A BIBLIOGRAPHICAL SOURCEBOOK OF COMPRESSED AIR, DIVING AND SUBMARINE MEDICINE

VOLUME II

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TO

THE SUBMARINERS, DIVERS, AND UNDERWATER SWIMMERS

OF THE

UNITED STATES NAVY

THIS VOLUME IS INSCRIBED

IN RECOGNITION OF

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PREFACE

THE publication of *A Bibliographical Sourcebook of Compressed Air, Diving and Submarine Medicine* in February 1948 provided a source of reference to the literature in medical problems of diving, compressed-air work, and submarine operations. Coverage in that volume extended to 1 January 1946. Since the appearance of the Sourcebook, the subject has rapidly advanced and hopes have been expressed that a second volume of the Sourcebook would be prepared. The encouragement of members of the Panel on Shipboard and Submarine Medicine of the Committee on Medical Sciences, Research and Development Board, Department of Defense, served as an important impetus to our undertaking the heavy task of bringing out this second volume. To facilitate the work, a contract (Nonr–199(00)NR 112–063) was negotiated and set up between the Office of Naval Research, Department of the Navy, and the Medical College of Virginia. This contract was effective between 1 November 1950 and 31 July 1953.

The literature cited in the present volume comprises pertinent unclassified reports and documents as well as published books, monographs, and papers appearing between 1 January 1946 and 31 December 1951. Because of the exigencies of war, it was impossible to obtain many items that should have been included in the first volume. These have subsequently become available and although they were published before the beginning of 1946, they have been included in the present volume for the sake of completeness. We have also added to the present volume all pertinent unpublished reports which appeared before 1 January 1946 and which have now been declassified. Some of these were open unpublished reports at the time of appearance. The reader will observe a number of new sections in the present volume which are not found in the first volume. In preparing these new sections, we have gone back and picked up contributory unpublished reports and published articles appearing before 1 January 1946.

The contents of the present volume have been handled according to the same policies that prevailed in assembling the first volume. In the text the observations and opinions of the investigators have been reported briefly and accurately, and all aspects of controversial issues have been considered. In our arrangement of the material and in our textual discussions, we have attempted to indicate research trends where these can be discerned.

As in the first volume, we have assigned a code symbol at the end of each entry in the bibliographical lists. *C* refers to classical or very early reports. *D* refers to discussion papers of a general character. *P* indicates articles reporting experimental investigations which have contributed to progress in the subject in question. *M* denotes recent papers presenting modern or current points of view. *R* designates review articles with comprehensive coverage. We have indicated with a *B* those reports with particularly useful bibliographies, and have designated with *Ch* those items which contain case histories.

ARRANGEMENT AND STYLE

The classification, arrangement, and style in the present volume follow the conventions observed in the first volume of this Sourcebook. We have assembled the references according to the scheme of subject-matter classification given below in the table of contents. As in the first volume, wherever unsigned articles are quoted, they are listed under "Anonymous" at the end of each subject group. A serial number has been assigned to each entry, and the reference is cited by this number in the index of authors and the text. We have followed the policy of spelling the surnames of authors as they appear in the original source in citing entries in the text and reference lists. In books and theses, the authors' names are given exactly as printed on the original title page. In citing papers in the journal literature and unpublished agency reports, only the initials

of given names are used. No attempt has been made to distinguish between male and female authors in citing papers and reports. In some cases, particularly in the French literature, an author's surname appears without given names or initials. In citing such items in the lists of references, the omission of the initials is indicated by square brackets following or preceding the surname.

The citation of published papers and books and other separate publications follows the style used in the first volume. Wherever possible, the title is given in the original language. Title translations of the romance languages are not provided. In all titles, the original language is used except in those languages requiring special alphabets. In such cases, if a translation into one of the commoner languages was supplied in the original article, this is quoted in the citation in parentheses. Wherever a new translation was made, this has been indicated by inclosing the translated title in square brackets. Whenever articles contain summaries in a second or third language, this information is given at the end of the citation.

In preparing citations of unpublished reports, we have followed insofar as possible the style for citation of published papers by placing the authors' names at the beginning of the citation if authors' names are given. In the citation of unpublished reports, the abbreviated name of the agency follows the subject title. In the case of those reports in which authors' names are not given, an abbreviated name of the agency is given at the beginning of the citation.

All journals and handbooks from which references have been taken are cited in a separate list at the end of this volume. These items are arranged in alphabetical order of their abbreviations, followed in each case by the full name of the publication. The system of abbreviations used conforms to *A World List of Scientific Periodicals published in the years 1900–1950, 3d edition, New York and London.* For journals not included in the *World List,* abbreviations have been created which conform to *World List* conventions and these abbreviations are followed by an asterisk in the journal list but not in the lists of references. In the Index of Authors, the names are listed in alphabetical order without distinction as to sole or joint authorship. In cases where variations of spelling of names are found, serial numbers are indexed under the commonest form of the name.

Following the Index of Authors, there is an Index of Sources for Unpublished Reports. Opposite each agency name are given the serial number or serial numbers of the reports by the agency in question. Following the Index of Sources for Unpublished Reports, a Key to Agency Abbreviations is included for the convenience of the reader.

ACKNOWLEDGMENTS

We desire to acknowledge with thanks our indebtedness for help, encouragement, and criticism to members of the staffs of the Bureau of Medicine and Surgery; the Office of Naval Research; the Medical Research Laboratory, U. S. Submarine Base, New London, Conn.; the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md.; the Experimental Diving Unit, U. S. Naval Gun Factory, Washington, D. C.; and the Naval Research Laboratory, Washington, D. C. Among the staff members of these naval activities, we particularly wish to thank Capt. O. E. Van Der Aue, (MC) U. S. Navy, Capt. Walter Welham, (MC) U. S. Navy, and Comdr. G. J. Duffner, (MC) U. S. Navy.

We were stimulated and encouraged to undertake the preparation of this volume through the initiative of Capt. C. W. Shilling, (MC) U. S. Navy. In all phases of the planning and execution of the work, Captain Shilling gave liberally of his time and shared freely with us his broad experience. His helpfulness in providing facilities and expediting plans have proved invaluable. His own deep concern for the advancement of naval research has been an inspiration to us and we wish to take this opportunity of expressing to him our grateful thanks.

We are especially grateful to Dr. Freeman H. Quimby, Head, Physiology Branch, Biological Sciences Division, Office of Naval Research, for his encouragement, understanding advice, and support. It is our privilege to express our appreciation to Dr. W. T. Sanger, president of the Medical College of Virginia, and to the staff of the College. We wish to record our gratitude to Maj. Gen. W. F. Tompkins, comptroller of the Medical College of Virginia, and his staff. To all of these, we would offer sincere thanks for continuing help and encouragement given us throughout the course of this project.

Lt. Edward H. Lanphier, (MC) U. S. Naval Reserve, Assistant Medical Officer, Experimental Diving Unit, U. S. Naval Gun Factory, Washington, D. C., gave generously of his time and energy in working with us in the planning and preparation of the section on special problems of swim-diving. We offer our grateful thanks to him.

We are deeply grateful to Prof. C. P. Yaglou, Harvard School of Public Health, for his helpful review and criticism of the sections on heat. We also desire to thank Dr. C. R. Spealman, Medical Divi-

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It is a pleasure to record our appreciation to Surgeon Commander Eric James, Royal Navy, for lists of names and copies of reports very kindly supplied by the British Admiralty. We also desire to thank Lt. Comdr. John Sebelien, Medical Corps, Norwegian Navy, for valuable advice on several overseas reference sources.

Most of the labor of assembling the literature included in this volume of the Sourcebook was conducted at the Armed Forces Medical Library, Washington, D. C. We desire to express our appreciation to Lt. Col. Frank B. Rogers, Director of the Library, for so generously placing at our disposal the facilities of the library during a period of over two years. Among the many members of the library staff who have helped us, we wish, in particular, to thank Mr. Kanardy L. Taylor, Dr. Estelle Broadman, Mr. Joseph C. Tucker, Mr. Robert B. Austin, Mr. Charles A. Roos, Mr. Edward A. Miller, Mr. Harold F. Koehler, Mr. H. Lynn Womack, Mr. Robert L. Carey, Mr. Joseph Bauer, and Dr. Anne Caldwell.

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We desire to express our grateful thanks to Mr. J. Heston Heald, head, Reference Section, Technical Information Division, Library of Congress. Mr. Heald and his staff provided us with a large volume of unpublished report literature. The generous aid offered by Miss Margaret McCluer, librarian of the Tompkins-McCaw Library, Medical College of Virginia, and the staff of the library is deeply appreciated.

The text of the present volume has been prepared using as source material special abstracts and translations prepared for this purpose. We have been assisted in this heavy task of preparing abstracts by Mrs. C. W. Shilling, Miss Betty Sugarman, Dr. Madeleine Wiener, Mr. Tibor W. Marton, Mr. Stanley Jablonsky, and Mr. Nils H. Randers-Pehrson. Our grateful thanks are extended to all of them for their willing cooperation.

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We desire to express our thanks to Mrs. Phebe M. Hoff for technical advice and assistance in developing the style for citation of unpublished references.

The work of making ready the manuscript for the press has involved many hours of diligent effort and close attention to detail. For devoted work on the manuscript, we wish to offer our sincere thanks to Miss Hagalyn H. Seay, Mrs. Delight Mathilda Hamilton, Miss Marguita B. Karson, and Mrs. Minna L. Hamner. We also wish to thank Chief Yeoman Jack Hamner, U. S. Navy, for his valuable assistance.

In a work of this magnitude, it is inevitable that errors and omissions will be found, although we have given minute attention to accuracy and completeness. The authors must assume entire responsibility for any deficiencies of the volume and will be grateful to readers who use it if they will draw our attention to mistakes that they may find. The opinions or assertions recorded herein are not to be construed as official or reflecting the views of the Department of the Navy or the naval service at large.

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SPECIAL ANATOMY, PHYSIOLOGY, ETC.—Continued

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General Studies of Submarine Medical Problems

THE references included in this section offer a comprehensive survey of the field. Papers by Behnke (*1* and *2*) 1947 and (*3*) 1951, and Benson and Behnke (*4*) 1951, give highlights of physiological research in service laboratories and also summarize the physiological and medical aspects of deep-sea diving. Willmon (*12*) 1949, (*13*) 1950, and (*14*) 1951, has discussed the relationships between medicine and engineering in submarines and has considered the effects of future submarine engineering developments upon the health of the crew. Medical problems of future submarines have also been considered by Yarbrough (*15*) 1948.

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14. Willmon, T. L. Man and the submarine. *J. Amer. med. Assn.*, 1951, *147:* 1028–1030.

15. Yarbrough, O. D. Medical problems of future submarines. *Milit. Surg.*, 1948, *102:* 342–346.

Technical Procedures and Research Apparatus in Compressed Air, Diving and Submarine Medicine

THE literature included under this title represents a selection of reference material and is admittedly not complete. The reports chosen are for the most part selected because they have been referred to in papers dealing with problems of compressed air, diving, and submarine medicine. The technical procedures and research apparatus described in these reports are therefore particularly relevant to the subject matter of this volume.

I. GENERAL STUDIES

Shilling and Kohl's chapter on submarine medical facilities and equipment (*16*) 1947 has been included and is suggested for readers who desire a complete list of medical equipment provided in the submarine.

16. Shilling, C. W. and J. W. Kohl. Submarine medical facilities and equipment. pp. 77–93 in: *History of submarine medicine in World War II.* U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. 25 May 1947, 328 pp.

II. GAS ANALYSIS IN AIR AND BLOOD

The references given below constitute the principal reports encountered in the compressed air, diving, and submarine medicine literature dealing with gas analysis in air and blood. These and other technical procedures are also referred to throughout this volume in other appropriate sections.

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80. Watkins, E., Jr. Rapid measurement of the oxygen saturation of whole blood samples with the Millikan oximeter. *Proc. Soc. exp. Biol., N. Y.,* 1949, *72:* 180–184.

81. Whiteley, A. H. A microvolumetric Van Slyke blood gas apparatus. *J. biol. Chem.,* 1948, *174:* 947–960. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 754. Abstr.

82. Young, A. C., L. D. Carlson, W. F. Quinton and H. L. Burns. Electronic polyneumograph. Electronic recording of tidal instananeous flow, respiratory rate, and minute volume with a gas sampling device for oxygen and carbon dioxide analysis in expired air. University of Washington, *Contract No. AF 33(038)–422, E. O. No. 211–01–021,* USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *AF technical rept. No. 6243,* March 1951, 17 pp.

III. RESPIRATORY APPARATUS

A limited number of respiratory devices are referred to in the reports which follow. For further details on respirators and other breathing appliances, the reader should consult the sections on deep-sea diving equipment and procedures (p. 289), resuscitation and respiratory devices (p. 290), and underwater breathing apparatus and related gear (p. 335).

83. Blockwick, T. N. Tests and evaluation of the Bendix and MSA O_2 breathing appliances for use in the recompression chamber. U. S. Navy. Naval gun factory, EDU. *Project NS–186–017, Rept. no. 12–49,* 21 October 1949, 16 pp.

84. Blockwick, T. N. Evaluation of the Scott type "A" oxygen demand inhalator. U. S. Navy. Naval gun factory, EDU. *Project NS–186–201, sub task no. 1, test no. C. rept. no. 5–51,* 14 March 1951, 5 pp.

85. Duncan, J. E. An improved helmet for breathing oxygen or other gases. *Science,* 1946, *104:* 395–396.

86. Forssander, C. A. A suction tube for the collection of respiratory gases under diverse conditions. *J. Lab. clin. Med.,* 1950, *35:* 324–327. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 60–61. Abstr.

87. Grove, G. W. and E. E. Quenon. Approval of newly developed self-contained breathing apparatus, instructions in its care and use and training procedure. U. S. Bureau of Mines. *Information Circular 7413.* July 1947, 18 pp. [R]

88. Hayter, R. Design and test of oxygen breathing equipment for use in the recompression chamber. U. S. Navy. NMRI. *Project X–540, Rept. no. 1,* 10 March 1947, 8 pp.

89. Kvacek, J. Otevren y okruh ve spirometrii. [The open circuit in spirometry.] *Cas. Lék. ces.,* 1950, *89:* 1030–1032. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 647. Abstr.

90. Miller, F., A. Hemingway, R. L. Varco, and A. O. C. Nier. Alveolar ventilation studies using the mass spectrometer. *Proc. Soc. exp. Biol., N. Y.,* 1950, *74:* 13–16. *Excerpta Medica.* Section II (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 301.

91. Pearce, S. J. and L. B. Berger. List of respiratory protective devices approved by the Bureau of Mines. U. S. Bureau of Mines. *Information Circular 7570.* June 1950, 15 pp.

92. Van Der Aue, O. E. and M. K. Holler. Tests and evaluation of various types of oxygen breathing equipment for use in the recompression chamber. U. S. Navy. Naval gun factory, EDU. *Project SRD 1162/47, Rept. no. 1,* September 1948, 15 pp.

93. Van der Valk, J. M. A simple method for the recording of human respiration. *Acta Physiol., Pharmacol., Neerl.,* 1950, *1:* 323–326. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 410.

IV. APPARATUS FOR TESTING VISUAL FUNCTIONS

For reports describing the uses of the apparatus and devices considered below, the reader should consult the section on visual problems (p. 119).

94. Draeger, R. H., R. H. Lee, and M. B. Fisher. Design, construction and preliminary evaluation of a portable multiple brightness radium plaque adaptometer. U. S. Navy. NMRI. *Project X–311, Rept. no. 1,* 11 August 1945, 16 pp.

95. Farnsworth, D. Abridgment and administration of the A. O. 1st edition pseudo-isochromatic plates. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–749 (Av–384–k), Color Vision Rept. no. 14,* 9 December 1946, 21 pp. [P]

96. Farnsworth, D. Standards for sunglasses. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.18, Rept. no. 4,* 6 pp. *Summer,* 1950, *20:* 81–87.

97. Farnsworth, D. Inspection goggle for checking visible spectral quality of lighting for dark adaption. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.40, Rept. no. 1,* 15 March 1951, 17 pp.

98. Grether, W. F., S. C. Connell, and J. M. Bjornstad. Experimental evaluation of the New London Navy Lantern for testing color perception. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero Medical laboratory. *Tech. rept. no. MCREXD–694–21B,* 1 March 1949, 11 pp. [P]

99. Hill, J. M. and F. T. Ralph. A penlight projector for the Lancaster red-green muscle test. *Amer. J. Ophthal.,* 1949, *32:* 1407.

100. Imus, H. A. Comparison of ortho-rater with clinical ophthalmic examinations. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine, *Project 499, Rept. no. 2,* 1 March 1946, 7 pp.

101. Koch, W. An improved dark-adaptometer. *Brit. J. Ophthal.,* 1947, *31:* 235–237. [P]

102. Krimsky, E. A new hand-slitlamp. *Amer. J. Ophthal.,* 1949, *32:* 1591–1592.

103. Lebensohn, J. E. A simplified astignometer. *Amer. J. Ophthal,* 1949, *32:* 1128–1130.

104. Lee, R. H., and R. H. Draeger. Design of a semiautomatic night vision scotometer. U. S. Navy. NMRI. *Project X–467, Rept. no. 1,* 2 July 1947, 4 pp. [P]

105. Lee, R. H. and M. B. Fischer. Evaluation of the modified Rostenberg adaptometer. U. S. Navy. NMRI. *Project X–466, Rept. no. 1,* 8 May 1945, 8 pp.

106. Littmann, H. A new slitlamp apparatus. *Amer. J. Ophthal.,* 1950, *33:* 1863–1870.

107. Pinson, E. A. and A. Chapanis. AML portable radium plaque night vision tester. *Air Surg. Bull.,* 1945, *2:* 285.

108. Raiford, M. B. Magnetic perimetry set. *Amer. J. Ophthal.,* 1950, *33:* 120.

109. Schmidt, I. A color signal apparatus for testing color vision in aviation. U. S. AAF. Heidelberg, Germany. Aero medical center. *Rept. P3–46–19,* Translated 26 May 1946, 10 pp.

110. Schober, H. Ein neues Adaptometer. *Klin. Mbl. Augenheilk.,* 1950, *117:* 51–58. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1295.

111. Von Schelling, H. and D. Farnsworth. Trichromatic specifications of the Munsell 100 hues at 5/5 for illuminant A. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 011 019, Rept. no. 3,* 15 April 1949, 8 pp.

112. Wolpaw, B. J. and H. A. Imus. Comparison of ortho-rater with clinical ophthalmic examinations. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine. *Project X–499, Final Rept.,* 29 September 1945, 26 pp. [P]

V. CHAMBERS

Literature that follows represents a selection from a large number of reports on pressure chambers. For applications of such equipment in compressed air, diving, and submarine medicine, the reader is referred especially to the section on decompression sickness (p. 159).

113. Blockwick, T. N. Test and evaluation of a portable recompression tank. U. S. Navy. Naval gun factory, EDU. *Project NS–186–024, Rept. no. 11–49,* 25 July 1949, 6 pp.

114. Brice, R. and P. Gaspa. Les nouveaux caissons à dépression mobiles du service de santé de l'air. *Med. aeronaut.,* 1950, *5:* 377–382.

115. Clarke, R. W. Yale refrigerated decompression chamber performance tests. Yale aeromedical research unit. *Rept. no. 10A,* 11 October 1942, 2 pp.

116. Davis, R. H. Deep diving with the Davis submerged decompression chamber. Oxy-helium diving by the Royal Navy. The Siebe, Gorman & Co. decompression tables. pp. 136–179 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., Fifth edition, 1951, 670 pp. [D]

117. Davis, R. H. Diving bells. pp. 197–203 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., Fifth edition, 1951, 670 pp. [D]

118. Gt. Brit., Ministry of labour and national service. Part V. Cofferdams and caissons. pp. 28–29 in: Factories acts, 1937 and 1948. *Work of engineering construction.* London, His Majesty's Stationery Office, 1951, 55 pp.

119. Siebe, Gorman and Company, Ltd. Recompression chamber for deep sea divers. *Descriptive information circular.* Siebe, Gorman and Company, Ltd., London, 2 pp.

120. U. S. Navy, BuShips. Preliminary instruction book. Submarine rescue chamber modified for deep submergence. *Navships No. 394–0051,* December 1949, 37 pp.

VI. AIR COMPRESSORS

The following reports on air compressors are included because of their particular pertinence in diving.

121. Davis, R. H. Standard diving apparatus and equipment with instructions for care, maintenance and testing. pp. 41–85 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., Fifth edition, 1951, 670 pp. [D]

122. Klimenko, N. A., K. A. Pavlovskii, and V. P. Maksimenko. Equipment of the diver. pp. 25–64 in: *Manual for divers of the navy.* Moskow, Military Printing Office, 1948, 172 pp. (Russian text.)

123. Molumphy, C. G. Preliminary volumetric test of lightweight diver's model no. SK 375 Dapco Air Compressor, test 2, priority "B." U. S. Navy. Naval gun factory, EDU. *Project SRD 805/47,* 26 January 1948, 6 pp.

124. Siebe, Gorman and Company, Ltd. Portable air compressing set for diving (two divers). *Descriptive information circular.* Siebe, Gorman and Company, Ltd., London, 2 pp.

125. U. S. Navy, Bureau of ships. Lightweight air compressor pp. 44–45 in: *Chapter 94, Salvage section II. Diving.* 25 January 1951, Washington, D. C., Government printing office, 1951.

VII. PRESSURE GAGES

The following references have been included since they have been mentioned in other reports published in this volume.

126. Brubach, H. F. and H. Specht. Barostat for high-altitude chamber. *Science,* 1951, *114:* 362–363.

127. Grundfest, H. A strain gage recorder for physiological volume, pressure and deformation measurements. *Science,* 1945, *101:* 255–256. [P]

128. Higgs, P. M. A recording mechanical pressure gauge of high range. *Rev. sci. Instrum.,* 1949, *20:* 23–26. [P]

VIII. TEMPERATURE MEASUREMENT

Most of the references that follow describe equipment discussed under the section on heat and humidity problems (p. 71) and the section on ventilating and air conditioning (p. 270).

129. Benzinger, T. H. and C. Kitzinger. Black body radiometer, a 4 pie receiver for measurement of total radiated heat output. U. S. NMRI. *Project NM 004.006.01(02),* 6 October 1949, 17 pp.

130. Challoner, A. R. and E. Griffiths. Experiments with the globe thermometer. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 45/254, H. S. 99,* December 1945, 3 pp. [P]

131. Hardy, J. D. and C. H. Richards. A new instrument for measuring the thermal radiation of the environment. *J. industr. Hgy.,* 1949, *31:* abstract section: 14. [P]

132. Jehn, K. H. Wet bulb temperatures without a wick. Electrical engineering research laboratory, University of Texas, *Contract N6onr–266, Task Order II, NR 082 005,* 1 September 1948, pp. 30.

133. Macradyen, A. A simple device for recording mean temperatures in confined spaces. *Nature,* 1949, *164:* 965–966. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1153.

134. Zahl, H. A. and M. J. E. Golay. Pneumatic heat detector. *Rev. sci. Instrum.,* 1946, *17:* 511–515.

IX. OTHER TECHNICAL PROCEDURES AND APPARATUS

A number of reports not classified elsewhere have been included in the list that follows.

135. Fisher, R. L. and W. A. White, Jr. The design of a circular slide rule for selecting decompression tables following compressed air dives. U. S. Navy. NMRI. *NH6–1/A11/NMRI–86,* 26 September 1944, 3 pp.

136. Houghton, F. C., W. A. White, Jr., and F. H. Davis. A study of the accuracy and reliability of the mine safety appliances carbon monoxide alarm. U. S. Navy. NMRI. *Project X–160, Rept. no. 3,* 8 July 1943, 6 pp.

137. Kramer, K. and D. E. Timmons. A photoelectric hypoxia warning device. *J. Aviat. Med.,* 1951, *22:* 70–74.

138. Van Slyke, D. D., J. R. Weisiger, and K. K. Van Slyke. Photometric measurement of plasma pH. *J. biol. Chem.,* 1949, *179:* 743–756. [P]

139. Wing, K. G. Suggestions for working with celloidin with special reference to the inner ear. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.27.01, Rept. no. 151,* 2 November 1949, 50 pp.

Special Anatomy, Physiology and Biochemistry of Compressed Air, Diving and Submarine Medicine

I. PHYSIOLOGICAL EFFECTS OF RAISED ATMOSPHERIC PRESSURES

A. CENTRAL NERVOUS SYSTEM

Generally speaking, personnel are capable of withstanding the effects of raised atmospheric pressures, per se, under conditions ordinarily encountered in compressed-air work and in diving. But the effects of pressure itself are not all that must be considered for it must be borne in mind that the caisson environment, for example, not only imposes raised atmospheric pressure upon the organism but also may involve factors such as increased humidity, extremes of temperature, inadequate ventilation, toxic gases, and heavy work in mud and cold water. Therefore, the physiological adjustments to be considered are, strictly speaking, not to be attributed to raised pressure alone. In deep-sea diving, pressures are reached at which oxygen intoxication becomes a severe and limiting factor. This problem is considered in an appropriate section (p. 182). At great depths there is a slowing of mental function and reduction of motor responsiveness attributed to the narcotic action of nitrogen under pressure. In both oxygen intoxication and nitrogen narcosis the effects upon the body are not to be ascribed to the influence of pressure itself, so that if nitrogen is replaced by helium, divers are capable of descending to much greater depths without adverse effects. It should also be remembered that at very high hydrostatic pressures, physiological processes are brought to a standstill and living protoplasm tends to become coagulated. A discussion of the biology of very high hydrostatic pressures is given on page 148. It is clear, however, that such pressures do not come within the range of possible effects on human beings. Within the pressure ranges at present encountered or likely to be encountered in diving or other underwater operations, increased pressure may be supported by living tissues without harm. Studies on dogs carried out by Rikkl and Krivosheenko (*140*) 1948 suggest that raised atmospheric pressure above two atmospheres gage pressure may exert inhibitory action upon the functions of the cerebral cortex. There appears to be an inhibition of condition reflexes.

140. Rikkl', A. V. and N. K. Krivosheenko. Vliianie povyshennogo atmosfernogo davleniia na vysshuiu nervnuiu deiatel'nost'sobaki. [The effect of increased atmospheric pressure on the higher nervous function of the dog.] pp. 62–69 in: *Trudy Nauchnoi Sessii, Posviashchennoi Tridtsatiletiiu Velikoi Oktiabr'skoi Sotsialisticheskoi Revolutsii.* Edited by A. V. Triumfov. Leningrad, Voenno-Morskoi Meditsinskoi Akademii, 1948, 310 pp.

B. HEART AND CIRCULATION

It may be concluded from earlier studies that raised atmospheric pressures do not produce very marked changes in cardiovascular action. On exposure to pressure, there tends to be a slight fall in pulse rate and blood pressure, although some reports have indicated a blood-pressure rise and sometimes an increase in pulse rate. Generally speaking, persons subjected to compressed-air work for long periods show no permanent change in blood pressure or cardiac function. Young and Cook (*142*) 1946, have investigated the effect of increased atmospheric pressure on blood pressure. Preliminary uncontrolled observations on 30 students at the School for Second-Class Divers, U. S. Submarine Base, New London, Conn., revealed an apparent drop in blood pressure during the 4 weeks' course. On the basis of these observations, an attempt was made to demonstrate, under controlled conditions, the effects on blood pressure of increased atmospheric pressure. A total of 60 subjects were exposed to raised atmospheric pressure. No ap-

preciable, lasting effect was demonstrated. The blood pressure was recorded on each subject before he got up in the morning and again at 1300. Subjects were seated 15 minutes before the reading and not permitted to smoke. The arm was placed at the heart level. Group A was exposed to a simulated pressure of 50 feet depth (reached in 4 minutes) and remained at this pressure for 3 minutes; subjects were then decompressed to 10 feet for 5 minutes and then surfaced. This was done for 13 days. Group B went through the same routine except that members of group B were not exposed to pressure. As stated, no appreciable effect of pressure on the arterial blood pressure was demonstrated. According to Farr, White, and Hayter (*141*) 1945, the specific gravity of whole blood or plasma of a group of 11 subjects did not change significantly following exposure to pressures as high as 10 atmospheres. In two subjects who developed symptoms of decompression sickness, significant changes were not observed in blood specific gravity before, during or after treatment for this disorder.

141. Farr, L. E., W. A. White, Jr., and R. Hayter. The effects of increased atmospheric pressure, posture and exercise on the blood specific gravity of normal men. U. S. Navy. NMRI. *Project X–443, Rept. no. 2,* 27 November 1945, 11 pp. [P]

142. Young, M. H. and W. E. Cook. The effect of increased atmospheric pressure on blood pressure. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–595,* 1 March 1946, 6 pp. [P]

C. RESPIRATION

Early investigations of the effects of raised atmospheric pressures on respiration have shown that daily exposure to increased atmospheric pressure produces a permanent increase in vital capacity. This claim was made by nearly all of the investigators interested in the use of raised atmospheric pressures for therapeutic purposes. However, more recent studies have thrown some doubt on this claim. Increase in vital capacity has been found but tends to be of low magnitude. Under raised atmospheric pressure, respiratory rate may be slowed and there may be an increase in breath-holding time.

Changes in alveolar carbon dioxide tension resulting from compression have been reported by Bean (*143*) 1945. Samples of air were drawn at the end of expiration from the lungs of anesthetized dogs by means of an implanted catheter. The first samples were taken at atmospheric pressure and compression of air was then carried to slightly over 5.5 atmospheres within 1.5 to 3.5 minutes. The second sample was taken just after maximum compression, the third a few minutes later. The pressure was then lowered to atmospheric level and a fourth sample taken. In 21 out of 22 compressions carried out on 4 animals, the carbon dioxide tension in the lung just after maximum compression was 10 to 85 percent higher than that obtaining before compression was begun. This increase in carbon dioxide tension was explained by the author as due to the compressional inflow of air into the lung preventing exhalation of alveolar air during the compression. Compressional inflow, according to the author, also tends to compress the alveolar air, thus temporarily elevating the carbon dioxide tension in immediate contact with the alveolar wall. It was concluded that the carbon dioxide thus dammed back in the blood and tissues constitutes an important etiological factor in those reactions which occur in highly compressed air, especially in the early stages and which have been attributed by some authors solely to a narcotic action of nitrogen. In 1950, Bean (*145*) also reported that rapid compression to 4.5 or 9 atmospheres resulted in a pronounced increase in alveolar carbon dioxide tension. These changes temporarily diminish and in some cases reverse the normal alveolar carbon dioxide diffusion gradient and dam up or drive back carbon dioxide into the blood. Although Bean did not categorically deny the possibility of nitrogen narcosis, he considered that his data showed that until the narcotic action of carbon dioxide is ruled out, substantial and conclusive evidence that nitrogen acts as a narcotic in the usual sense of the term is wanting. Bean (*144*) 1947 compressed anesthetized, heparinized dogs in air to about 90 pounds pressure in 3 or 4 minutes. During compression there was a shift of the arterial pH in the acid direction. Rapid decompression produced the reverse effect. The compressional shift was explained by the author as due to interference with carbon dioxide removal. The decompressional pH changes were held by the author to have important implications relative to explosive decompression, rapid ascent to high altitudes, and rapid decompression from high pressures.

143. Bean, J. W. Changes in alveolar carbon dioxide tension resulting from compression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1945, *4:* 6.

144. Bean, J. W. Changes in arterial pH induced by compression and decompression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 76–77.

145. Bean, J. W. Tensional changes of alveolar gas in reactions to rapid compression and decompression and question of nitrogen narcosis. *Amer. J. Physiol.,* 1950, *161:* 417–425. [P]

II. PHYSIOLOGICAL EFFECTS OF DECOMPRESSION FROM PRESSURES HIGHER THAN ONE ATMOSPHERE

A. GENERAL STUDIES OF THE EFFECTS OF DECOMPRESSION

Eggleton, Elsden, Fegler, and Hebb (*146*) 1945 and Specht (*147*) 1948 provide a general introduction to the problem of the effects of decompression from pressures higher than one atmosphere. The source material given in this section makes available information applicable to the study of the etiology of decompression sickness and its prevention and treatment.

146. Eggleton, P., S. R. Elsden, J. Fegler, and C. O. Hebb. A study of the effects of rapid "decompression" in certain animals. *J. Physiol.,* 1945, *104:* 129–150. [P] [D]

147. Specht, H. Physiological effects of abnormal atmospheric pressure. pp. 135–174 in: *Industrial Hygiene and Toxicology.* Edited by F. A. Patty. New York, Interscience Publishers, Inc., 1948. [R]

B. PHYSIOLOGY OF BUBBLE FORMATION

For a comprehensive discussion of the genesis of the tissue bubble, Fulton's chapter (*159*) 1948 should be consulted by the reader. Reference should also be made to a report by Catchpole and Gersh (*157*) 1946 on the physical factors in the pathogenesis of aeroembolism. These inclusive and well-prepared reviews will serve as a guide to orient the reader to the vast literature on the subject of bubble formation.

For experimental observations on the actual formation of gas bubbles in blood vessels and tissues following decompression from high-pressure atmospheres, papers by the following should be consulted: Gersh (*161*) 1945, Gersh and Hawkinson (*165*) 1944, Gersh, Hawkinson, and Jenney (*166*) 1944, Gersh, Hawkinson, Rathbun, and Behnke (*167*) 1944, and Wagner (*192*) 1944. In Wagner's experiments gas bubbles were observed directly in pial blood vessels following rapid decompression of anesthetized cats from air compressed to 75 lbs. per sq. in. (gage pressure). When gas bubbles were visible in the pial vessels, they always appeared first in the arteries and later in the veins. Gas bubbles were also present in other blood vessels of the body as well as in the right auricle and ventricle. Some animals died although no bubbles appeared in the pial vessels of the microscopic field under observation. Since in all animals the distribution of gas bubbles elsewhere in the body was the same, it was assumed that in those instances in which gas bubbles were not seen under the field, they were actually present in arteries supplying portions of the central nervous system other than the field under observation. Since gas bubbles appear in pial arteries before they appear in the veins and since distribution occurs in other vessels irrespective of their appearance in pial vessels, it was concluded by the author that pial gas bubbles are borne to their site of lodgment as gas emboli. Secondarily, as the blood flow through the region decreases, gas bubbles appear in the veins.

The object of the experiments of Gersh and Hawkinson was to describe the origin, occurrence, and appearance of tissue and vascular bubbles in fat tissue, adrenal glands, nerve, liver, skeletal muscle, and tendon after decompression from high atmospheric pressures. Adult guinea pigs in good nutritional state were used in these studies. The animals were kept for 60 minutes in a small pressure tank at 30, 45, 60, 75, 90, or 105 lbs. per sq. in. (gage pressure) and decompressed in 4 seconds. Extravascular gas bubbles were observed in tissues rich in fat, adrenal cortex, and nerve fibers, but were not seen in liver, skeletal muscle, or tendon. Intravascular bubbles were observed in all these tissues and organs, but were far more numerous in those rich in fat. The number, size, and location of extravascular bubbles appeared related to the total fat content of the fat tissue. Although tissue bubbles showed the same distribution in the tissues and organs of fat and lean guinea pigs, it was found that they occurred much more readily and were far more extensive in the fat animals than in the lean ones. Gersh, Hawkinson, Rathbun, and Behnke found a significant fall in the specific gravity of guinea pigs after decompression from high pressures. This fall was greater in fat animals than in lean animals and was attributed to the presence of gas bubbles. Gersh, Hawkinson, and Jenney compared the occurrence of bubbles following decompression from high-pressure atmospheres of oxygen, helium-oxygen, argon-oxygen, and air. In fat tissue, extra-vascular gas bubbles occurred in the order of decreasing frequency following decompression from high-pressure atmospheres of argon-oxygen, air, oxygen, and helium-oxygen. Intracellular gas bubbles were observed after decompression from argon-oxygen, air, and helium-oxygen, but not from oxygen alone. Intravascular bubbles were present with all gas mixtures. In the adrenal cortex, gas bubbles occurred in the order of decreasing severity following decompression from high-pressure atmospheres of argon-oxygen, air, and helium-oxygen atmospheres. After decompression in oxygen only occasional bubbles were seen. In the myelin sheath of nerve fibers, minute bubbles were more numerous following decompression from argon-oxygen than from compressed air and less numerous after decom-

pression from helium-oxygen and oxygen. In the liver, intravascular gas bubbles were common after decompression from argon-oxygen, rare after air and helium-oxygen, and absent when oxygen was used. In the hepatic cells, cytoplasmic watery vacuoles were present following decompression from all gas mixtures. Gas bubbles were not found in muscle fibers or tissue fluid spaces of skeletal muscles after decompression in any of the gas mixtures. Bubbles were present intravascularly after argon-oxygen, air and helium-oxygen, air and helium-oxygen mixtures, though not after oxygen. Survival of guinea pigs decompressed from high-pressure atmospheres was favored with gas mixtures in the following order; oxygen, helium-oxygen, air, and argon-oxygen. The relative effects of decompression from various gas mixtures may be explained by differences in solubility in oil and in water, in the oil-water solubility ratios and in the diffusibility of the gases and permeability of the tissues.

Gersh (*161*) 1945 reported studies on gas bubbles in bone and associated structures as well as in the lung and spleen of guinea pigs decompressed rapidly from high pressure atmospheres. In bone, small numbers of gas bubbles were found and these only in the veins and the sinusoids of bone marrow of the tibia after exposure of guinea pigs to compressed air for one hour. After exposure for 3 hours both intravascular (artery, vein, and sinusoid) and extravascular disruptive gas bubbles were visible. In some animals the Haversian systems of bone were occluded by gas columns. Periostial blood vessels were only occasionally distended with gas. Gas bubbles were also found in the blood vessels of the tendon sheaths near the ankle and knee joint, but were more numerous in the former. These findings are related by the author to aseptic bone necrosis of caisson workers and to theories of the origin of the pain of bends. In the lungs gas bubbles were found only in the pulmonary artery and its branches, stretching the walls of the medium-sized and small vessels. These findings are related to theories as to the origin of the pain of chokes. Gas bubbles were found in decreasing order of frequency in the sinusoids, arteries, and veins of the spleen of guinea pigs decompressed after exposure to compressed air. Their origin is related to the peculiarities of the vascular system of the spleen and to the occurrence of vascular emboli.

Gersh (*160*) 1945 and (*162*) 1946 carried out investigations designed to correlate X-ray and gross observations on gas bubbles in guinea pigs decompressed from high atmospheric pressures. The animals were compressed at 75, 90, and 105 lbs. per sq. in. (gage pressure) for 1 to 1½ hours and decompressed in 4 seconds. Medium-fat and fat animals were used. X-rays of the extended left hind leg were made of each animal before and after decompression. Following the second X-ray the animals were autopsied and the distribution of gas bubbles in the body observed grossly. In animals that died following decompression, X-rays of the leg revealed radio-translucent lines corresponding to the larger veins. The regions occupied by fat between the hamstring muscles or in the inguinal regions became somewhat radio-translucent with a clear outlining of lymph nodes present in the fat depots. Except in one instance, no evidence was found of patterns suggesting bubbles. Yet such bubbles ranging from 0.05 to 0.7 mm. in diameter were seen in large numbers in these areas on gross examination at autopsy. In the X-ray plates there was no evidence of the bubbles which were found on gross examination to be present along the course of, but outside of, the larger blood vessels. Many bubbles were found in the inguinal fat. It was concluded that bubbles in blood vessels are recognizable in X-rays, while bubbles in fat or other forms of connective tissue are usually recognizable only as a general X-ray shadow. Tissue bubbles or extravascular bubbles are rarely identifiable as such, probably because of a combination of the following factors: the small size of the bubble, poor resolution, and overlay. Failure to recognize bubbles in the X-rays of men suffering from bends may, according to the author, result from limitations of the X-ray method and cannot be interpreted as indicating the absence of gas bubbles intravascularly or extravascularly.

X-ray examination of animals following decompression from high pressures has also been carried out by Colonna and Jones (*158*) 1948. These authors commented that X-rays provide a crude means for early detection of manifestations of caisson disease in bones. Autopsy of animals that died following decompression showed numerous air bubbles in the venous circulation, in fat and subcutaneous tissues, the mesentery, fascial planes, and mediastinum. The lungs were congested and the heart dilated. Cavities were consistently found in the bone marrow, both grossly and microscopically, presumably formed by large bubbles collecting in the soft marrow of the long bones. Early evidence of a permanent defect in bony tissue was present following repeated decompression. The author interpreted the changes in the bones of the rabbits used in these experiments as an early stage in the production of asceptic necrosis of bone.

A series of reports has been given by Gersh and Catchpole on bubble formation in rabbits decom-

pressed to altitudes. These authors (*163*) 1945 and (*164*) 1946 made gross observations on rabbits decompressed after a 10-second period of preoxygenation to a simulated altitude of 45,000 feet. The animals were prepared for histological studies at 30,000 feet, the tissues being frozen in situ with isopentane chilled to −150° C., or removed with all blood vessels clamped and then frozen by immersion into the chilled fluid. When animals died as a result of decompression, bubbles were found only in the blood vessels. No extravascular bubbles were seen. Bubbles were seen with equal frequency in the arteries and veins in all tissues and organs studied. They occurred chiefly in the relatively large vessels, and the only capillaries containing gas were those in the fat tissues. Gas bubbles in the kidney were never seen in vessels smaller than the interlobular vessels. The largest vessels occluded with gas were those in the fatty tissue. Little gas was found in the fascial planes of skeletal muscle. Gas bubbles were present in the sinusoids of the spleen and some in the bone marrow. They were absent in the sinusoids of the liver and adrenal cortex. Very few bubbles were seen in the pulmonary vessels. Only one bronchiolar vessel contained gas. Epineural and intraneural vessels were occluded by gas bubbles.

Catchpole and Gersh (*154*) 1945, (*156*) 1946, carried out an investigation to determine the effect of preoxygenation, electrical stimulation, anesthesia, carbon dioxide, sodium bicarbonate, lactic acid, and ammonium chloride on bubble formation in rabbits decompressed to reduced atmospheric pressures. It was found that 30 minutes of preoxygenation before decompression to a simulated altitude of 45,000 feet permitted rabbits to survive while the controls died. Respiratory gas mixtures containing 5 and 10 percent carbon dioxide failed to affect survival. The beneficial effects ascribed to carbon dioxide at altitude do not extend to the prevention of aeroembolism. Intraperitoneal injections of sodium bicarbonate were likewise ineffective. Intraperitoneal administration of ammonium chloride and of lactic acid prevented death from aeroembolism. Electrical stimulation of a hind limb with resulting muscular contractions at altitude caused the death of animals decompressed to a simulated altitude and at a decompression rate at which unstimulated controls survived. Conversely, muscular immobilization by nembutal anesthesia tended to favor survival.

In a further study on the physiological factors affecting the production of gas bubbles in rabbits decompressed to altitudes, Catchpole and Gersh (*153*) 1945 and (*155*) 1946 found that decompression time had an important influence on bubble formation at altitude. Rapid decompression led to a high incidence of bubbles and early death, while slow decompression gave low bubble incidence and late death or survival. At the critical decompression time of 10 minutes to reach a simulated altitude of 45,000 feet, 80 percent of the animals survived for 30 minutes after reaching altitude, while with decompression times of less than 10 minutes, 80 percent of the animals died with vascular bubbles in 30 minutes or less after reaching altitude. Bubble incidence and time of death were unrelated to body fatness, previous activity, spontaneous activity at altitude, body weight, and the sex of adult animals. Very few bubbles were found in the coronary arteries or pulmonary system. The authors considered that the probable cause of death was embolism of the central nervous system.

As to other physiological factors affecting experimental bubble formation, Wedral and Ivy (*191*) 1941 have examined the relation of circulatory rate to aeroembolism and aeroemphysema. The relation of temperature and exercise to bubble formation in rats and in torniqueted legs of rabbits and goats has been reported by Reed and Blinks (*186, 188*) 1944 and Reed, Blinks, and Pease (*189*) 1944. In dead animals or in tourniqueted legs, low temperature protects against bubble formation and is the controlling factor in preventing bubbles in decompressed animals. Low temperature over a period of several hours protected against bubbling regardless of motion, and high temperatures facilitated bubbling even in the absence of motion. In living animals, however, exercise is the important factor over the tolerated temperature range, the latter having little effect. The main temperature effect seems to be upon the rate of carbon dioxide production in anaerobic glycolyses. Both carbon dioxide and nitrogen are significant in bubble formation and resistance, the former acting as a facilitator. If nitrogen is previously removed by preoxygenation, few or no bubbles occur. According to Reed and Blinks (*187*) 1944, vasoconstriction does not enhance bubbling in the blood. Vasodilatation apparently protects somewhat against bubble formation but only if the animal is taken very slowly to altitude allowing time for nitrogen to be flushed out.

For a further study on various physiological factors affecting bubble formation in animals, a paper by McElroy, Whiteley, Cooper, Pease, Warren, and Harvey (*183*) 1944 should be consulted.

A large number of studies have been carried out on the physical conditions for the formation and growth of gas bubbles. For such studies, reports by Bateman (*148 and 149*) 1942 should be consulted.

A long series of reports by Harvey and coworkers likewise provide essential and definitive source material on this subject. In 1942, Harvey, Cooper, Pease, McElroy, and Whiteley (*174*) showed that pure water or aqueous solutions, including blood, supersaturated under 8 atmospheres with air or carbon dioxide, can remain so without bubble formation indefinitely, provided they are free of a preformed gas phase in the form of small gas masses or gas nuclei. Any kind of gas or even water vapor itself may serve as a nucleus for visible bubble formation from any other kind of gas, but without these minute gas nuclei, no visible bubbles are formed. These small gas nuclei stick to any dirty, especially greasy surfaces in vitro and by growth are converted into bubbles or series of bubbles which detach themselves. In 1943, Harvey, Cooper, Pease, McElroy, and Whiteley (*175*) described a device for detecting bubble-forming nuclei in the blood of mammals. No nuclei were found in the carotid blood of nembutalized cats and dogs at ground level, at altitude or under decompression. This indicates that nuclei do not enter through the lung membrane or form in lung capillaries. Possible turbulence near the heart is not a factor in bubble formation of the quiet animal. Bubbles can form in water free of gas nuclei as a result of movement by pressure pulses, shock waves, sound waves, turbulence, Reynolds' cavitation effects, and tearing of a liquid. Gas nuclei greatly favor bubble formation under these conditions, as does dissolved gas and low initial pressure on the liquid. In still, supersaturated water, gas nuclei seem to be the only source of bubbles.

According to Harvey, Barnes, McElroy, Whiteley, and Pease (*173*) 1944, the conventional method of removing gas nuclei by prolonged boiling or evacuation has the disadvantage of removing dissolved gas in addition to the gas nuclei. It was found that strong centrifuging of the liquid and the container will remove gas macro nuclei so that no bubbles form when the liquid is evacuated to the vapor pressure of water. Also, previous exposure of liquid and container to high hydrostatic pressures (10,000 to 16,000 lbs. per sq. in.) will remove all gas nuclei from a liquid by forcing them into solution.

For other studies on bubble formation, papers by Harvey (*169*) 1945, (*170*) 1950, (*171*) 1951, and (*172*) 1951; Harvey, Cooper, Pease, McElroy, Whiteley, and Warren (*176*) 1943; and Harvey, McElroy, Pease, Whiteley, Warren, Barnes, and Kleinberg (*177*) 1943 should be consulted. Of special interest is a report by Harvey, Whiteley, Cooper, Pease, and McElroy (*178*) 1946 on the effect of mechanical disturbance on bubble formation in single cells and tissue after saturation with very high gas pressures. In these studies cells and tissues were placed in small glass dishes in a shallow layer of liquid and exposed to pressures of 152, 80, and 76.5 atmospheres in a steel chamber with glass windows so that observation of the material could be made through a microscope. Amebae were subjected to 75 atmospheres for 2 hours, paramecia were exposed to 78 atmospheres for 2 hours. Various other cells were also used. In those studies in which precautions were taken to remove external gas nuclei by preliminary high hydrostatic pressure treatment (16,000 lbs. per sq. in. for 2 hours), no bubbles appeared in the water or on the outside or inside of the cells on decompression, although the cells themselves died. Cells without prepressure treatment formed many bubbles on the outside, demonstrating that bubble formation is dependent on gas nuclei which are found on the outside of the cell. The formation of gas in single living cells is considered unusual even after decompression from high nitrogen pressures or decompression to high vacuums.

Fresh rat tissues subjected to 16,000 lbs. per sq. in. for an hour to remove all gas nuclei were subsequently compressed to 40 to 80 atmospheres for 15 to 30 hours and afterwards decompressed to atmospheric pressure. Bubbles arose in the fat, in skeletal muscle, and in fragments of clotted blood. Copious extracellular bubbles were observed deep within the fat tissue. A very few intracellular bubbles were seen only when the pressure difference was greater than 50 atmospheres. Decompression of fat tissue after saturation with 20 atmospheres of nitrogen was not enough to elicit intracellular bubbles although large intercellular bubbles did appear. Stretching the connective tissue with glass needles after decompression resulted in more abundant bubble formation. This burst of bubbles was believed to be due to the separation of the surfaces previously in contact. At the moment of separation a "dry" spot is left into which a few dissolved molecules diffuse before water can again cover the region. The gas molecules act as gas nuclei which quickly grow under the conditions of high supersaturation. The tearing of one surface from another must result in formation of a small cavity into which gas molecules diffuse before collapse can occur. This small group of gas molecules constitutes a gas nucleus. Such a mechanism is considered to be involved in formation of bubbles in animals and man in decompression sickness.

A definitive article on bubble formation in liquid is that of Harvey published in 1950 (*170*). Physical factors in bubble formation are also considered by Harvey in a chapter published in 1951 (*171*). In

summarizing the problem, Harvey states that pressure differences are regarded as the driving force for bubble formation, while the size of the bubbles and rate of formation are largely determined by gas diffusion which depends not only on pressure difference, but also on surface area, diffusion constants, and particularly on gas solubility. Gas nuclei or rough surfaces may act as generators for new bubbles. Bubbles can easily form in blood vessels because the endothelium is hydrophilic. The author refers to all nuclei which grow at or above vapor pressure of water as gas macronuclei and those requiring a greater pressure difference for growth as gas micronuclei. For de novo formation of bubbles in a homogeneous liquid at rest containing dissolved gas, it is necessary that the pressure difference be of the order of 100 to 1,000 atmospheres. Techniques for demonstration of gas bubbles involving the freezing of decompressed tissues for histological study are questioned by the author on the grounds that bubbles may arise from surfaces of rapidly formed ice crystals. If a nitrogen bubble is surrounded by a solution of carbon dioxide at the same tension, the bubble will grow because carbon dioxide diffuses in much more rapidly than nitrogen can diffuse out. Possibly respiratory movements, heart beat, circulation, or peristalsis are responsible for local tensions than cause bubble formation. It appears that bubbles can arise from tissues in the complete absence of gas micronuclei and that gas micronuclei are unnecessary for bubble formation under conditions that might be important in the body. In a chapter on bubble formation in cats, Harvey (*172*) 1951 states that an altitude of 45,000 feet seems to be the critical altitude in cats for bubble formation. Muscle contraction introduces two factors, both of which favor the early formation of bubbles under all conditions: Excess carbon dioxide production and decreased hydrostatic pressure resulting from the mechanical tension developed. One of these factors, the decreased hydrostatic pressure, becomes particularly important at altitude because the animal is already near the vapor pressure of water.

Regarding the role of carbon dioxide as a facilitating agent in the initiation and growth of bubbles in animals, papers by Blinks, Twitty, and Whitaker (*152*) 1951 and Harris, Berg, Whitaker, Twitty, and Blinks (*168*) 1945 should be consulted. These authors believe that carbon dioxide greatly increases the ease with which bubbles may be initiated and may be responsible for their rapid growth in early stages of development. At later stages nitrogen is more directly concerned with their further growth and development. Dead rabbits and frogs were found to bubble profusely on decompression to simulated high altitudes. This was attributed primarily to accumulation of carbon dioxide derived from residual cellular respiration after death and from anaerobic glycolysis with attendant decomposition of bicarbonates in blood and tissue fluids. If anaerobic glycolysis was inhibited by using sodium iodoacetate as the lethal agent, bubble formation was greatly reduced or lacking on subsequent decompression. Administration of carbon dioxide in high concentrations to living frogs lowered the minimum altitude at which bubble formation occurred with exercise. Pretreatment with carbon dioxide also reduced the degree of muscular activity necessary for bubbles to form in frogs at high altitudes. Bubbles from decompressed rats were found to contain as much as 60 to 80 percent carbon dioxide. It is believed that as bubbles move out into larger vessels, there is loss of carbon dioxide and increase in nitrogen which is responsible for the further growth and maintenance of the bubbles.

For further studies on bubble formation, papers by the following may be consulted: Berg (*150*) 1945–46; Berg, Harris, Whitaker, and Twitty (*151*) 1944; Hill (*179*) 1951; Horiuti (*180*) 1946; Lemaire (*181*) 1947; McElroy and Whiteley (*182*) 1946; Pease, Blinks, and Reed (*184*) 1944; Piccard (*185*) 1944; and Rodbard (*190*) 1946.

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159. Fulton, J. F. Decompression sickness. The genesis of the tissue bubble. pp. 51–90 in: *Aviation medicine in its preventive aspects. An historical survey.* London, Oxford University Press, 1948, 174 pp. [R]

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161. Gersh, I. Gas bubbles in bone and associated structures, lung and spleen of guinea pigs decompressed rapidly from high pressure atmospheres. U. S. Navy. NMRI. *Project X–284, Rept. no. 10,* 10 May 1945, 12 pp. [P]

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C. SATURATION AND DESATURATION OF GASES IN THE BODY

The elimination of nitrogen from tissues and fluids of the body is of particular significance as a factor in bubble formation. The references included in this section have been chosen because of their value as source material in connection with the section on decompression sickness (p. 159). For studies of nitrogen elimination, the following references may be consulted: *193, 194, 195, 196, 197, 198, 200, 203,* and *209.* The reader should consult a review by Kety (*199*) 1951. This article discusses the theories and formulas which have been offered to explain and calculate exchange of inert gases in the lungs and tissues.

For theoretical papers on blood-tissue exchange of inert gases, reports by the following should be consulted: Morales and Smith (*204*) 1944, (*205* and *206*) 1945, and (*207*) 1948; Morales, Smith, and Behnke (*208*) 1945; and Smith and Morales (*213*) 1944. For studies on neon, argon, krypton, xenon, and radon, papers by the following should be consulted: Lawrence, Loomis, Tobias, and Turpin (*201*) 1946; Smith and Labaw (*212*) 1948; Tobias, Jones, Lawrence, and Hamilton (*215*) 1949; and Turpin, Loomis, Lawrence, Jones, and Tobias (*216*) 1945. Carbon dioxide elimination and the effect of carbon dioxide on the rate of denitrogenation have been investigated by Margaria and Sendroy (*202*) 1950, Schaefer and Scheer (*210*) 1951, and Sendroy and Margaria (*211*) 1950. For a study of denitrogenation of muscle and fat tissues, a paper by Whiteley and McElroy (*217*) 1946 may be consulted. The rate of nitrogen elimination from the body through the lungs has been investigated by Stevens, Ryder, Ferris, and Inatome (*214*) 1947.

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D. FAT AND WATER CONTENT

Fats and water are so distributed in the body that during saturation a large part of the nitrogen absorbed by fat diffuses from the body fluid. During decompression following partial saturation, the diffusion of nitrogen from the rapidly saturating body fluids into slowly saturating lipoids and fats tends to equalize the partial pressure of nitrogen in the different tissues of the body. After short exposures to high pressures, the fat acts as a nitrogen absorbent during decompression and serves as a buffer against bubble formation in the bloodstream. According to Behnke (*193*) 1945, fat men with adequate blood supply and circulation should be better suited for short exposures in compressed air than lean men. In view of these facts and the differential solubility of nitrogen and other inert gases in fats as distinct from fluids, importance has been attached to studies of the fat and water content of the body. The references given in this section constitute the principal reports on this subject.

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III. PHYSIOLOGICAL EFFECTS OF LOW OXYGEN TENSIONS OF ENVIRONMENTAL AIR

A. LOW OXYGEN PERCENTAGES WITHOUT DECOMPRESSION

1. SPECIAL SENSES

Experimental and clinical findings as well as results of operational experience reveal a deterioration of acuity of function of special senses under conditions of hypoxia. Continued submergence may lead to a reduction in oxygen percentage in the submarine air that may cause sensory loss. Only a few reports in this field are included here.

Of interest experimentally are the lenticular opacities produced in rats and rabbits by hypoxia. These so-called hypoxic cataracts have been discussed by Morone and Citroni (*246*) 1950. These authors call attention to disturbances of anaerobic glycolysis of the crystalline lens both during and at the end of the opacification phase and even when no opacification occurs. Pretreatment did not alter the frequency of occurrence or severity of hypoxic cataracts. Scano, Bietti, and Schupfer (*248*) 1947, have studied the modifications of the retinal resolving power under conditions of hypoxia produced by the rebreathing method. There was a reduction of 6 percent in the retinal resolving power until an oxygen percentage corresponding to an altitude of 5,000 meters had been reached. At lower oxygen percentages a diminution of about 12 percent was observed. For a report on reduction of fusional amplitude in human subjects breathing low oxygen mixtures (8.5 to 10 percent), a paper by Bietti and Giardini (*239*) 1949, may be consulted. Bietti and Scano (*240*) 1948, subjected normal subjects to hypoxia by breathing an air mixture containing 8.3 percent oxygen. In these subjects there was an increase in the contraction speed of the pupil as well as the dilatation speed. Aniseikonia appeared as an inconstant finding. In some subjects the mydriatic pupil could not be excited. Changes in the visual field during oxygen deficiency have been reported by Ikui, Nakano, and Hosio (*245*) 1947, and Smith, Seitz, and Clark (*249*) 1946, have discussed variations in the angioscotoma in response to prolonged mild anoxia. In these experiments subjects were exposed for 7½ hours in a low oxygen mixture corresponding to an altitude of 10,000 feet. There was a progressive and significant increase in the size of scotoma observed. It became more marked at the end of 7½ hours. The time course of failure of the visual pathway in rabbits during nitrogen breathing has been reported by Noell and Chinn (*247*) 1949. In these studies the potentials resulting from illumination of the eye and from electrical stimulation of the optic nerve were recorded from different parts of the visual pathway. The curves for decline in responsiveness revealed complete unresponsiveness at the surface of the striate area of the occipital cortex following either photic or electrical stimuli after 88 seconds of nitrogen breathing. For further studies of the effect of hypoxia upon the visual mechanism, papers by Giulio (*243* and *244*) 1948, may be consulted.

Wever, Lawrence, Hemphill, and Straut (*250*) 1949 have examined the effects of oxygen deprivation upon the cochlear potentials. They measured electrical potentials generated in the cochlea during stimulation with sound (1,000 cycles) under normal conditions and in the course of oxygen deprivation. Cats under Dial anesthesia were curarized to the point where reflexes were absent and spontaneous respiration ceased. They were maintained by artificial respiration. Cochlear potentials were picked up from the membrane of the round window and measured by a selective voltmeter. Low oxygen mixtures produced a progressive deterioration of the potentials, and there was a delay in recovery of such potentials after air breathing was reestablished. Bornschein and Krejci (*241*) 1950 in experiments on guinea pigs also showed a depression of the cochlear potentials during hypoxia. They found that this depression is independent of the frequency of the auditory stimuli. The sensitivity of the cortical auditory projection area to hypoxia has been investigated by Gellhorn (*242*) 1951. In these experiments cats were subjected to an air mixture containing 7.5 percent oxygen. The auditory and

visual cortical potentials were found to be about equally sensitive to hypoxia. Breathing oxygen-nitrogen mixtures containing 7.5 percent oxygen led to a distinct and nevertheless reversible diminution of the visual and auditory responses due apparently to a reduction in the number of responding neurons.

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240. Bietti, G. and A. Scano. Ricerche di pupillografia in anossia. *Riv. med. aero., Roma,* 1948, *11:* 177–209. (English, French, Spanish, and German summaries.) [P]

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248. Scano, A., G. B. Bietti, and F. Schupfer. Influenza dell'anossia sul potere risolutivo retinico. *Rev. Med. aero., Roma,* 1947, *10:* 490–498. (Italian, English, French, Spanish, and German summaries.)

249. Smith, G. M., C. P. Seitz, and K. B. Clark. Variations in the angioscotoma in response to prolonged mild anoxia. *J. Aviat. Med.,* 1946, *17:* 590–595. [P]

250. Wever, E. G., M. Lawrence, R. W. Hemphill, and C. B. Straut. Effects of oxygen deprivation upon the cochlear potentials. *Amer. J. Physiol.,* 1949, *159:* 199–208. [P]

2. NERVOUS SYSTEM

Effects of hypoxia on peripheral nerve activity have been reported by the following: Aykut and Winterstein (*251*) 1950; Beyne, Chauchard, and Chauchard (*252*) 1948; Fenn and Gerschman (*269*) 1950; and Laget, Lavigne, and Gaillard (*279*) 1951.

The effect of asphyxia on the monosynaptic pathway through the spinal cord has been investigated by Brooks and Eccles (*255*) 1947. Changes were observed in the monosynaptic pathway obtained by means of a needle electrode in the quadriceps nucleus at the rostral end of the sixth lumbar segment of the cord. Orthodromic volleys were excited by way of the sixth dorsal root or the nerve to the quadriceps after severance of motor fibers. Antidromic excitation was produced by stimulation of the deafferented quadriceps nerve of the sixth ventral root. Asphyxia produced by stopping the artificial respiration, causing the heart to fail, or clamping the thoracic aorta gave brief depression followed by a period of hyperexcitability attributable to depolarization of the membranes of the afferent nerve fibers and the motoneurone somas. Continued asphyxiation caused progressive depolarization with final failure of impulse propagation. The effect of anoxia and hypoxia as well as carbon dioxide upon the monosynaptic and multisynaptic reflex discharges in spinal and decerebrate cats was investigated by Kirstein (*278*) 1950. Monosynaptic and multisynaptic reflex volleys in the ventral roots at the seventh lumbar and first sacral levels elicited by stimulation of the afferent fibers from the gastrocnemius and anterior tibial muscles and the sural nerve were examined. Both in anoxia produced by administration of pure nitrogen, and in ischemia produced by clamping the abdominal or thoracic aorta, the monosynaptic reflex showed an initial depression followed by a period of augmentation. In long-standing anoxia and ischemia the reflex was eventually depressed. In some experiments the initial decrease was preceded by a transient facilitation. Interruption of anoxia or ischemia during the period of maximal facilitation brought about an immediate depression of the reflex. The multisynaptic response behaved differently, showing a gradual depression sometimes preceded by a transient augmentation. The depression of the multisynaptic reflex always occurred later than the initial depression of the monosynaptic reflex. Both anoxia and ischemia gave the same results, indicating that the effects observed were due to oxygen deficit and not to carbon dioxide excess. A mixture of 7.9 percent oxygen in nitrogen produced only depression in nearly all cases. A mixture of 8.9 percent carbon dioxide in oxygen caused pure depression in all cases. With both mixtures, the depressant effect was more pronounced in the monosynaptic than in the multisynaptic reflex system. In the studies of Brooks and Eccles (*255*), oxygen lack (7 to 10 percent oxygen) had the same effect as asphyxia except for

absence of early transient depression of activity which precedes the phase of hyperexcitability. Sudden readmission of oxygen during the period of asphyxial or anoxic hyperexcitability resulted in depression. Carbon dioxide excess (11 to 14 percent) produced pure depression of the monosynaptic pathway in Brooks and Eccles' experiments. Accumulation of carbon dioxide was seen to explain early depression in asphyxia.

Gellhorn (*271*) 1943 has pointed out that when animals are subjected to progressive degrees of hypoxia, there is first a respiratory reaction (increase in ventilation) and that only with more severe degrees of hypoxia does the blood pressure rise. Experiments indicated that the chemoreceptors act more efficiently on the respiratory than on the vasomotor center. If the carotid sinus is removed, the animal shows respiratory failure which is accompanied by a striking fall in blood pressure. If the respiratory failure is prevented by artificial respiration in an animal with pneumothorax, the blood pressure rises in hypoxia. Chemoreceptors from the sinoaortic area excite both vasomotor and respiratory centers. The two centers are different inasmuch as the removal of the carotid sinuses alone produces respiratory failure in hypoxia whereas, in order to obtain a similar failure of the vasomotor apparatus (fall of blood pressure in anoxia), all four buffer nerves must be removed. In spite of the depression of the vasomotor center in hypoxia it still reacts with a slight rise in blood pressure to stimulation from higher parts of the central nervous system. The depressor reflexes are weakened in hypoxia. Hypoxia may produce a syndrome similar to that observed in orthostatic hypotension. The blood flow through the extremities in hypoxia is the resultant of the centrally controlled vasoconstriction and the local dilating effect. The former predominates particularly under more severe degrees of hypoxia. The tissues incur an oxygen debt which is paid off after readmission of air. The significance of the excitation of the sympathetic system lies in the rise in blood pressure which provides a more adequate circulation to the brain and heart at the expense of the extremities and of the visceral organs. This action on the brain is supplemented by the dilating effect of hypoxia on the brain vessels. The sympathetic effects are intensified by the secretion of adrenalin.

Hypoxia leads to a lowering of the temperature of the body. This reaction greatly increases resistance to hypoxia, since hypoxia more rapidly becomes fatal when the lowering of the body temperature is prevented. In a further report on the medulla oblongata in hypoxia, Gellhorn (*272*) 1948, concluded from the physiological literature that in chronic hypoxia respiration and possibly blood pressure are regulated through the medullary centers alone. These data were adduced to explain how even mild degrees of chronic hypoxia may have fatal effects if they act on diseased medullary neurons. In experiments of Malmejac and Chardon (*284*) 1946, dogs breathed an air mixture containing 6 to 10 percent oxygen in nitrogen with the carotid sinuses denervated. In some experiments crossed circulation was established with a donor dog. These studies of the resistance to hypoxia of the respiratory center, the vasomotor center, and adrenal secretions showed that the latter is most resistant to hypoxia. In the terminal phase the respiratory center was most vulnerable; cessation of respiratory movements preceded the beginning of severe terminal cardiovascular effects. In a further series of experiments, Malmejac, Chardon, Neverre, and Fontanille (*289*) 1948, found that, in dogs inhaling air containing only 4 percent oxygen, there was a diminution of carotid sinus excitability during the first stage, but in the second stage syncope of the respiratory center predominated. According to Cordier and Cordier (*258*) 1950, there was no alteration of the sensitivity of the respiratory center during hypoxia (oxygen concentrations of 4.26 to 8.60 percent) in animals deprived of the chemoreceptors and the stellate ganglia and inferior cervical ganglia.

Effects of hypoxia on the vasomotor center have also been reported by Malmejac, Chardon, and Gross (*285, 286, 287,* and *288*) 1948. The carotid sinus in hypoxia is considered to play a double role, mechanical and chemical, the latter being much more important and more durable (*285*). The vasoconstrictor reactions are nervous in origin. The chemical action of the carotid bodies causes a peripheral vasodilatation and a central vasoconstriction. Sudden hypoxia may cause a transient excitation of the vasomotor centers. To demonstrate this central action, Malmejac, Chardon, and Gross (*286*) used a dog in which one of the hind legs was perfused by a donor. The dog was curarized and its vasodepressor nerves cut and artificial respiration induced. At a given moment a mixture of nitrogen and oxygen was substituted for the air in the respirator. Under these conditions it was seen that 1 to 3 minutes after respiration of a mixture with 2 to 3 percent oxygen, the perfused hind limb showed a vasoconstriction. Respiration of mixtures with more than 5 to 6 percent oxygen did not cause this effect. The same authors (*287*) pointed out that oxygen

lack ultimately produces a progressive breakdown of the vasomotor centers. In the terminal stages of hypoxia the vasocontrictor tone of central origin is, however, somtimes reestablished.

In a discussion of the brain and the symptomatology of hypoxia, Himwich (*275*) 1949, gives evidence of the high sensitivity of the upper cortical centers to oxygen lack. If one accepts the concept of a metabolic gradient in the central nervous system, it follows that not all parts of the brain will be equally affected by hypoxia, but that those regions with the highest metabolic rates will succumb first and those with the lowest will be last. Gradual progression down the phyletic centers reveals the release of control of cortical areas giving unhampered expression to lower centers. During a slow, progressive hypoxia, contact with the environment is first lost. There is then aimless motor restlessness followed by torsional spasms and then tonic spasms with flexion of the arms and extension of the legs as the midbrain is released. Finally opisthotonus is seen. Cold, clammy skin follows, with a feeble heart, depressed respiration, and finally muscular flaccidity.

For further study of differential effects of hypoxia upon the nervous system, reports by Noell and Chinn (*291*) 1950 and (*292*) 1951, may be consulted. In rabbits, potentials were recorded from different parts of the visual pathway in response to flashes of light into the eye and to electrical stimulation at various levels during suddenly induced anoxia. Inexcitability involved first the cortex, next the geniculate bodies, then the retinal ganglian cells, then the bipolar cells, and finally the photoreceptors. The propagation of excitation towards the bipolar cell level induced by a light stimulus survived anoxia for about 20 minutes as indicated by the appearance of an electronegative retinogram. The measured survival time of the retinal ganglian cells was about 5 minutes; that of the geniculate cells and the most resistant cortical neurons about 2 minutes. When strong light stimulus was applied, conduction across the retinal ganglian cell layer was nearly as resistant to anoxia as optic nerve conduction. Similarly, conduction across the geniculate synapses failed only slightly earlier than conduction of the geniculocortical fibres. Summation, facilitation, or inhibition were in many instances early affected by anoxia. The authors suggested that the rapidity with which a central mechanism involving numerous neuronal chains is impaired by anoxia depends largely upon properties of its functional organization rather than on the true anoxic resistance of its neuronal members as measured by inexcitability or blockage of impulse conduction.

The effect of anoxia upon electrically induced convulsions has been investigated in rabbits by Dahlberg-Parrow (*265*) 1951. It was found that hypercapnia produced by pretreatment for 5 minutes with 12 percent carbon dioxide in oxygen prolonged the flexion stage of the gastrocnemius muscle in electrically induced convulsions and shortened the subsequent extensor phase. The total tonic phase was shortened. Conversely, the succeeding clonic phase was prolonged and a clonic phase produced in animals normally having none. Under anoxia (pretreatment for 10 seconds with 100 percent nitrogen) the tonic phase was shorter and in most animals the clonic phase was absent. The duration of seizure was shortened markedly by anoxia in animals normally having no clonic phase or only a short one. The author concluded that in such animals central anoxia may be the factor for discontinuation of convulsive activity. Gellhorn and Heymans (*273*) 1948, found in cats and dogs that inhalation of 4 percent oxygen in nitrogen abolished convulsive potentials from the cortex at a time when normal potentials were practically unchanged. On readmission of air, normal potentials were found to appear in previously convulsive areas before convulsive spikes reappeared. Asphyxia induced by cessation of artificial respiration likewise abolished spikes before normal potentials and lead to earlier reappearance of the latter on readmission of air. The data indicated to the authors that hypoxia and asphyxia induce progressive decruitment of cortical cells and reoxygenation a progressive recruitment. The limiting factor which determines the number of discharging neurons and degree of their activity, whether convulsive or nonconvulsive, seems to be the supply of oxygen. Restitution of normal oxygen supply after hypoxia or asphyxia is often accompanied by a rebound phenomenon with convulsive potentials appearing which were absent under control conditions. Regarding the effects of low oxygen on the cortical potentials as recorded in the electroencephalogram or the electrocorticogram, Brazier (*254*) 1946, found in human subjects that lowering the oxygen concentration of the inspired air slowed the rate of cortical potentials. The slowing was greater the lower the oxygen level. The greatest slowing occurred when both the oxygen and carbon dioxide content were low. The electroencephalograms of psychoneurotic patients showed a greater degree of slowing than did those of normal adults, suggesting a more labile metabolic process in the cortical cells of psychoneurotic patients than in normal persons. Iwama (*277*) 1950–51, also reported changes in the electroencephalogram in human

subjects breathing low oxygen mixtures. In these studies the subjects breathed 6 or 7 percent oxygen for 5 minutes. Within a minute after the start of the hypoxic period, small, rapid waves appeared. Two to three minutes later, there were slow, large delta waves appearing in groups. The mean amplitude increased rapidly. The final stage contained almost all delta waves. In oxygen lack of slight degree, the potentials were markedly suppressed at an early stage. In rabbits exposed to a 12-percent oxygen mixture, the electrocorticogram showed an increased amplitude of the predominant rhythm with a frequency of about 5 cycles per second from studies reported by Crossland and Richter (*264*) 1950. Hypoxia in these experiments produced a fall in brain acetylcholine.

For studies of the effect of hypoxia upon psychological functions, papers by the following may be consulted: Fabre and Rougier (*267*) 1946, Fletcher (*270*) 1945, Lovett-Doust (*281*) 1951, Smith (*298*) 1946, Smith and Seitz (*299*), 1946, and Waldfogel, Finesinger, and Verzeano (*302*) 1950. A report on the effect of low oxygen on psychological performance tests in psychoneurotic patients and normal control subjects has been given by Waldfovel, Finesinger, and Verzeano (*302*) 1950. Psychoneurotic patients and control subjects were given psychomotor tests while breathing 21 percent oxygen and while breathing 10 percent oxygen, the total period of exposure to low oxygen tension being about 20 minutes. The average performance in both the patients and the control groups dropped in almost every instance despite the counteracting effects of practice. This general downward trend is consistent with other studies of the effects of hypoxia upon performance. The control subjects dropped more on the reaction time tests while the patients showed a greater drop on the tapping speed and stylus tests. However, when the two groups were compared directly with one another in regard to the amount of change produced by hypoxia, it was found that there was no statistically significant difference between them. The two groups were compared also as to the appearance of physical symptoms. It was found that they were very much alike in type, frequency, and severity of symptoms reported. The only difference was that the controls seemed to experience headaches and giddiness more frequently, while the patients experienced more difficulty in breathing and more tremor and unsteadiness. Smith and Seitz (*299*) 1946 and Smith (*298*) 1946 have shown that hypoxia produced by breathing low oxygen mixtures results in deterioration in speech intelligibility. In subjects exposed to oxygen mixtures simulating an altitude of 10,000 feet for an 8-hour period, the decrement in speech intelligibility was slight and unreliable at the 45-minute period. There were more marked effects at the 2¼- and 4¾-hour periods and considerable lessening of the altitude effect 6¾ hours after entering the chamber. The tests indicated that the loss of efficiency under the conditions of the experiments was primarily due to subjective factors such as wandering attention and boredom. The subjects reported that there was an increase in somnolence and greater boredom in the altitude runs than in the control runs. It thus seems apparent that even relatively mild degrees of hypoxia may result in significant losses of speech intelligibility which may affect performance.

For studies of the pathological effects of hypoxia upon the nervous system, papers by the following should be consulted: Courville (*259, 260* and *261*) 1947, Courville (*262* and *263*) 1950, Douglas (*266*) 1949, Morrison (*290*) 1946, Petrov (*294*) 1949, and Plambeck (*295*) 1950. In a series of contributions to the study of cerebral hypoxia, Courville (*259–263*) has described pyknotic changes, liquefaction, vacuolation, and lipoid degeneration in nerve cells. Interstitial cells are less affected. In acute cases, small, perivascular hemorrhages are often found. The cortex and basal ganglia and the choroid plexus and pia mater are filled with blood. Courville has pointed out (*263*) that the effect of hypoxia on the nervous system is not generalized, but that certain areas are more susceptible than others. These susceptible areas include the globus pallidus and other nuclei of the basal ganglia. The pathological changes in the basal ganglia may be designated as the key lesion of hypoxia. Some transitory and reversible effects of hypoxia may be evidenced by Parkinsonian manifestations and emotional flattening. This may disappear after weeks or months. Chronic exposures result in changes in the myelin sheaths, the demyelinization being patchy and the sheaths swollen. It appears that the hypoxic state provokes a vascular spasm of sufficient duration to result in physical changes in the myelin sheaths. In reporting histopathological changes in the brain of a man deprived of oxygen for a period of 5 to 10 minutes, Douglas (*266*) 1949 described severe degenerative changes in the cerebral cortex (particularly in the motor and visual areas), in the putamen, and in the cerebellum. In both the precentral and visual cortex there was considerable softening. In dogs and monkeys exposed to hypoxia for considerable periods, Morrison (*290*) 1946 found that the degree and duration of hypoxia is correlated with progressive necrosis and cellular exhaustion. The first histological changes occur in the granular cells

of the supragranular layer of the cortex at a level of about 12 or 13 volumes percent of oxygen in the blood. At 10 volumes percent and down to 4.5, there was progressive chromatolysis, swelling, vacuolation, and massive laminar necrosis in the gray matter, and at this point the white matter showed signs of blanching, demyelinization, gitter cell formation, and microglial hyperplasia. There was a certain amount of reversibility upon restoration of normal oxygen tension. The order of effect in decreasing severity was found to be: the frontal lobe, the parietal lobe, the occipital lobe, the temporal lobe, the basal ganglia, and the cerebellum. No injury to the cord was observed at oxygen tensions compatible with life.

For further studies on the physiological and pathological effects of low oxygen pressures on the nervous system, papers by the following may be consulted: Binet and Strumza (*253*) 1950, Callebaut, Rodbard, and Katz (*256*) 1950; Cerletti and Kallenberger (*257*) 1948; Fender, Neff, and Binger (*268*) 1946; Grenell and Kabat (*274*) 1947; Iandolo (*276*) 1947; Loeschcke (*280*) 1948–49; Lowenback (*282*) 1951; Lucas (*283*) 1946; Petrov (*293*) 1949; Royer and Thiebaux (*296*) 1951; Sloan (*297*) 1950; Steegmann (*300*) 1951; and Volochov and Obraszova (*301*) 1950.

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3. MUSCULAR ACTIVITY

Daoud and Wilson (*303*) 1950, have shown that subjects breathing air containing 12 percent oxygen suffer a definite loss in muscular strength, as measured by the pressure of a squeezed ball held in the hand. There is loss both of the strength of an initial maximal effort and a muscular effort sustained for 1 minute. This decrement becomes very striking at oxygen percentages below 9 percent, and with 8 percent there is 100 percent loss. For studies on the effect of complete anoxia on contractility and metabolism of intestinal smooth muscle, two papers by Furchgott and Shorr (*304, 305*) 1950 and 1948 may be consulted.

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4. HEART AND CIRCULATION

Early cardiovascular responses to hypoxia involve changes which tend to compensate for reduced oxygen tension and enhance circulatory efficiency. There may be acceleration of the pulse, increased cardiac output, elevation of systemic arterial blood pressure, and vasoconstriction in certain viscera.

When the degree of hypoxia exceeds the limits of toleration, cardiovascular collapse supervenes.

The effects of hypoxia upon the electrocardiogram have been widely investigated. A few selected reports are included here (*316, 326, 338, 351* and *356*). Of interest is a report by Hoyos (*338*) 1949 in which rabbits were exposed to sudden anoxia by various drastic methods. There was first a sinus tachycardia with a normal or shortened P–R interval. This was succeeded by sinus brady-cardia with prolonged P–R interval and deviation of the S–T segment. In the final agonal stages, the QRS complexes become monophasic, large and wide. Sometimes a partial A–V block was found. The first phase of sinus tachycardia is probably a compensatory effect and nervous origin. The third or agonal phase is due to the direct action of anoxia upon the myocardium. The second phase is probably due to the combined effects of anoxia of the myocardium and of secondary vagotonia.

In studies of cardiac output in acute anoxia Feldman, Rodbard, and Katz (*327*) 1949 demonstrated that after the onset of nitrogen breathing in anesthetized dogs, the blood flow nearly doubles in the superior vena cava, with a lesser increase in the inferior vena cava. Within 70 seconds there is a rise of blood pressure of 10 to 40 mm. Hg. After the blood pressure began to fall from its peak value and when it had almost returned to its control value (after 100 seconds), the flow in the inferior vena cava suddenly fell to nearly zero, although the flow in the superior vena cava was almost undiminished. With the resumption of air breathing, there was a rapid return of flow in the superior and inferior venae cavae with a striking rise in blood pressure.

Continuous exposure to simulated altitude may result in cardiac dilatation, according to Grandpierre and Franck (*334*) 1947. This paper contains 69 references to dilatation and hypertrophy of the heart due to hypoxia. The extreme sensitivity of cardiac muscle to hypoxia is well established. In experiments by Lemley and Meneely (*341*) 1951, the oxygen uptake was measured in homogenized myocardial tissue from rats exposed to acute hypoxia produced in a decompression chamber. The animals were subjected to an atmosphere equivalent to 7 percent oxygen for 1 hour and killed by exposure to an equivalent of 3 percent oxygen. At the moment of respiratory arrest the hearts were removed, homogenized in buffered saline solution, and the oxygen uptake measured. It was found that homogenized myocardial tissue from rats exposed to hypoxia used only one-half as much oxygen as homogenates from normal animals. The oxygen consumption of homogenates from hypoxic hearts was increased threefold by addition of an extract of boiled myocardial tissue. Boiled-heart extract from both normal and hypoxic animals produced this increase, but the former was slightly more effective than the latter. Grundmann (*337*) 1950 exposed cats to air mixtures containing 6 to 8 percent oxygen until death. There was acute edematous swelling of the myocardium with infiltration of the wall of the cardiac arteries. Blood-pressure changes in the right and left ventricles associated with a reduction of oxygen tension in the inspired air in dogs have been investigated by Gauer and Kramer (*330*) 1948. As the tension in the inspiratory air decreased from 200 mm. Hg. to 48 mm. Hg, the systolic pressure in the ventricles and carotid arteries increased.

Pulse-rate changes in response to hypoxia have been reported by the following: Chardon, Gross, and Fourrier (*318*) 1947; Chardon, Gross, and Fourrier (*319*) 1947; Dahlene (*321*) 1948; Dripps and Comroe (*322*) 1946; Efimov (*325*) 1942; Georg and Sonne (*331*) 1947; and Steinmann and Konig (*359*) 1951. Cardiac acceleration resulting from hypoxia is mediated partly by augmentation of cardioaccelerator nerve activity, partly by diminution of moderator tone, and partly by adrenalin secretion (*318, 319*). According to Dripps and Comroe (*322*) 1946, there are no measureable circulatory responses in human subjects to 18 percent oxygen. Some subjects show a slight but definite response to 16 percent oxygen, and this is noticeable in pulse-rate changes. Acceleration of the pulse is thus one of the earliest physiological responses to hypoxia. Other studies (*325, 331* and *359*) indicate that pulse-rate increase is a constant finding in hypoxia of sufficient intensity to evoke any compensatory responses.

It is well known that an early compensatory physiological response to hypoxia is provided in the contraction of the spleen. In recent studies of Luft and Kramer (*342*) 1950, changes in spleen weight and in the hemoglobin content of systemic blood were recorded during acute hypoxia in nembutalized dogs. Contraction of the spleen occurred regularly in these authors' experiments; however, the response did not appear early but was a terminal event immediately preceding respiratory failure. Loss in spleen weight during its contraction coincided with an increase in systemic hemoglobin content. During the refilling phase of the spleen after hypoxia, the same inverse relationship was evident when systemic hemoglobin returned to the initial level. An estimate of the hemoglobin concentration in the stored blood in the spleen based on the

amount of blood released by the spleen and the subsequent increase in total circulating hemoglobin gave a figure of approximately 40 grams percent. This implies that the splenic stores consist almost entirely of packed red cells. Continuous records of the hemoglobin content in the splenic vein showed very rapid changes in the final stages of hypoxia with peak values twice as high as in the arterial blood. During recovery, the hemoglobin level in the splenic vein was slightly lower than in the artery. Spontaneous rhythmic fluctuations in the hemoglobin content of the splenic vein were frequently observed in the control periods. The oxygen saturation remained consistently higher in the splenic vein during hypoxia than in the arterial blood, and even improved when splenic contraction reached its peak. In the critical phase of hypoxia, the spleen of the dog releases a large number of red cells with a relatively high oxygen content into the portal venous system.

Alella (*306* and *307*) 1950 and 1951 studied in human subjects the effect of hypoxia on the velocity of the pulse wave. Hypoxia did not affect the velocity of the pulse wave in the aorta, but, in general, the velocity in the femoral and tibial arteries is increased. This is presumed to be due to variation in muscular tone of these latter arteries and not to blood-pressure changes accompanying hypoxia.

Alteration in the lesser circulation as a result of hypoxia has been investigated by the following: Atwell, Hickam, Pryor, and Page (*309*) 1951; Beard, Alexander, Howell, and Reissmann (*310*) 1951; Bierman (*315*) 1951; Duke (*323*) 1951; Duke and Killick (*324*) 1950; Motley, Cournand, Werko, Himmelstein, and Dresdal (*352*) 1947; Nahas, Mather, Hemingway, and Visscher (*353*) 1951; Nisell (*355*) 1951; and Wescott, Fowler, Scott, Hauenstein, and McGuire (*368*) 1951.

The influence of short periods of acute hypoxia upon pulmonary artery pressures in man has been reported by Motley, Cournand, Werko, Himmelstein, and Dresdal (*352*) 1947. Pulmonary hypertension was rapidly induced in subjects with normal blood pressure by breathing 10 percent oxygen for short periods of time with only a very slight rise in systemic blood pressure. The pulmonary pressures rapidly returned to normal when low oxygen breathing was discontinued. Cardiac output was decreased slightly during hypoxia and the stroke volume markedly reduced. Pulmonary vascular resistance was almost doubled during hypoxia while the systemic peripheral resistance increased only slightly. Westcott, Fowler, Scott, Hauenstein, and McGuire (*368*) 1951 have examined the effects of hypoxia on the human pulmonary circulation by means of cardiac catheterization. Breathing 13 percent oxygen caused an average rise in mean pulmonary artery pressure of 24.6 percent above control levels. No significant change in the mean pulmonary capillary pressure was observed in subjects who breathed 13 percent oxygen. No statistically significant change in cardiac output could be attributed to hypoxia in subjects in whom multiple Frick determinations were made. Simultaneous determinations of mean pulmonary artery and pulmonary capillary pressures and cardiac output were made before, during, and after 13 percent oxygen breathing. The pulmonary arteriolar resistances calculated therefrom showed an average increase of 48.5 percent during the low oxygen breathing, a difference which was shown to be highly significant statistically. Duke and Killick (*324*) 1950 and Duke (*323*) 1951 have examined pulmonary vasomotor responses to hypoxia, hypercapnia, and other conditions in a study of perfused isolated cat lungs (*323*). It was found that pulmonary vasoconstriction was produced by inhaling gas mixtures containing 5 to 10 percent carbon dioxide or gas mixtures containing less than 15 percent oxygen. Pressor responses in the pulmonary arterial system were found under both conditions. Ventilation of the lungs with pure oxygen had no effect in these experiments. Ventilation of the lungs with pure neon or hydrogen produced effects similar to those produced by pure nitrogen. Pulmonary vasomotor responses to carbon dioxide and oxygen lack were not abolished by dihydro-ergotamine or atropine. Since dihydro-ergotamine and atropine did not affect the pulmonary vasomotor responses to carbon dioxide or hypoxia, it seemed unlikely that adrenergic or cholinergic nervous elements were involved. The available evidence seemed in favor of the change in alveolar air composition exerting a direct effect upon some part of the pulmonary vascular bed. Nisell (*355*) 1951 reported reduction in pulmonary vascular resistance during perfusion of hypoxic or hypercapnic blood through the cat lungs. This effect was concluded to be due to a dilatation of the pulmonary arteries or arterioles. The constriction of the pulmonary vessels following inhalation of gas deficient in oxygen or containing carbon dioxide presumably occurred in the venules or veins. A reduction in blood flow through the hypoxic lung has been reported by Atwell, Hickam, Pryor, and Page (*309*) 1951. Studies were made of individual lung blood flows in the dog when both lungs breathed air and when one lung breathed air while the other was in equilibrium with the pulmonary arterial blood by rebreathing while the other lung continued to breathe air, half the animals showed a shift of pulmonary blood flow

through the air breathing lung and away from the rebreathing lung.

The influence of short periods of acute hypoxia upon pulmonary artery and left atrial pressures in dogs has been investigated by Nahas, Mather, Hemingway, and Visscher (*353*) 1951. Pressures in the left atrium and pulmonary artery of the conscious animals were recorded by means of strain gage manometers when the animals breathed room air and after breathing a mixture of 8 percent oxygen in nitrogen for 10 minutes. On room air the average mean integrated pressure in the left atrium was 5.8 mm. Hg (range 1 to 11.2 mm. Hg). The pressure in the pulmonary artery was 18.2 mm. Hg (range 13 to 22.5 mm. Hg). The average cardiac output was 3.3 liters per minute. After the dogs had breathed 8 percent oxygen in nitrogen for 10 minutes, the mean integrated pressure of the pulmonary artery rose in all cases. The average rise was 5.2 mm. Hg (range 2 to 8 mm. Hg). The pressures in the left atrium remained the same or fell slightly. During the same period the average cardiac output fell from 3.3 down to 2.3 liters per minute, a 30 percent drop. The average oxygen consumption fell from 171 cu. cm. per minute to 109 cu. cm. per minute, a 36 percent fall. The average carbon dioxide production rose from 121 cu. cm. per minute to 176 cu. cm. per minute, a 31 percent increase. The average respiratory quotient rose from 0.72 up to 2.6. These results, confirming previous interpretations, indicated to the authors that the increase in pulmonary pressure occurring during short periods of acute hypoxia truly results from a vascular change taking place in the pulmonary vascular bed. In contrast, Beard, Alexander, Howell, and Reissmann (*310*) 1951 found no significant change in pulmonary arterial pressure in dogs after 15 minutes of exposure to a mixture containing 8.5 percent oxygen.

Reduction of oxygen percentage in the respired air results in disturbances of visceral circulation and in particular in the circulation through the kidneys. Franklin, McGee, and Ullmann (*328*) 1950 have reported that, in rabbits and other animals, acute anoxia produced a marked diversion of the renal cortical blood flow in the innervated, but not in the denervated kidney. Direct observation of the kidney during anoxia showed a generalized paling, diminution in size of the organ, and wrinkling of the capsule. Brull and Divry (*317*) 1950 have shown that when anoxemia combines with poor venous output so that the amount of available oxygen in the kidneys drops from normal levels above 0.25 down to below 0.10 ml. per gram of kidney per minute, urinary secretion practically stops. Kreienberg, Prokop, and Schiffer (*340*) 1949 found that decrease in the oxygen supply resulted in a striking decrease in renal blood flow correlated with a degree of hypoxemia. The renal blood flow was found to be dependent on systemic blood pressure. When normal air breathing was resumed, there was an additional renal blood-flow decrement and then the flow rate began to rise slowly, taking a long time to return to normal. Addition of 1.2 to 3 percent carbon dioxide to the air mixture intensified and hastened the decrement of renal blood flow during hypoxemia.

For further studies of the effects of hypoxia upon heart and circulation, papers by the following should be consulted: Anderson, Allen, Barcroft, Edholm, and Manning (*308*) 1946; Bernthal (*311*) 1947; Bernthal, Greene, and Reufin (*312*) 1951; Bernthal and Woodcock (*313*) 1951; Betourne (*314*) 1950; Comroe and Dripps (*320*) 1950; Feldman, Rodbard, and Katz (*327*) 1949; Frey (*329*) 1948; Gordon and Turner (*332*) 1951; Grandpierre and Franck (*333*) 1947; Grandpierre, Franck, and Lemaire (*335*) 1949; Grandpierre, Franck, and Lemaire (*336*) 1950; Huerkamp and Rittinghaux (*339*) 1950; Malmejac and Chardon (*343*) 1947; Malmejac and Chardon (*344*) 1949; Malmejac and Chardon (*345*) 1951; Malmejac, Chardon, and Gross (*346*) 1949; Malmejac, Chardon, and Neverre (*347*) 1949; Malmejac, Chardon, and Neverre (*348*) 1949; Malmejac, Chardon, and Neverre (*349*) 1949; McMichael and Snyder (*350*) 1943; Nairn (*354*) 1951; Scano (*357*) 1947; Scardigli (*358*) 1949; Surtshin, Rodbard, and Katz (*360*) 1947; Surtshin, Rodbard, and Katz (*361*) 1948; Swann and Brucer (*362*) 1949; Swann and Brucer (*363*) 1949; Swann and Brucer (*364*) 1949; Swann and Brucer (*365*) 1949; Van Loo, Surtshin, and Katz (*366*) 1948; Vannotti (*367*) 1946; and Woodcock (*369*) 1945.

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5. BLOOD

For studies on the effects of hypoxia on the blood, papers by the following may be consulted: Berk, Burchenal, Wood, and Castle (*370*) 1948; Cordier and Coudier (*371, 372*) 1950; Germanov (*373*) 1949; Magnussen (*374*) 1949; Malmejac, Cruck, and Neverre (*375*) 1948; Penneys, Thomas, and Lewis (*376*) 1950; Reissmann (*377*) 1950; Riska (*378*) 1950; Rosin and Rachmilewitz (*379*) 1948. Studies on the production of erythrocytes in vitro (*374* and *379*) have indicated that the maximum production occurs at oxygen percentages from 10 to 30 percent. Rosin and Rachmilewitz found that gas mixtures containing 1, 3, 5, 10, and 12 percent oxygen have an injurious effect on hemic cells in the bone marrow of rabbits in vitro. The bone marrow showed various degrees of degeneration, more pronounced at the lower oxygen percentages. Bone marrow cultures in 15 percent oxygen did not show any appreciable changes and were similar to controls in normal air. Berk, Burchenal, Wood, and Castle (*370*) 1948 measured the oxygen saturation of sternal marrow blood in human subjects. In general, no significant differences were demonstrated between normal subjects, convalescent control subjects, anemic patients, and patients with polycythemia vera. In some patients with leukemia and with myeloid metaplasia and in some patients with polycythemia vera with evidence of excessive myeloid activity, the data suggested an increased local oxygen utilization relative to the blood flow in the bone marrow. However, it was concluded that the techniques used were not adequate to demonstrate a hypoxic stimulus to increased erythropoiesis, even in the marrow of patients with chronic anemia, probably because of the difficulty of obtaining blood samples satisfactorily representative of the undisturbed environment of the erythropoietic tissue. Reissmann (*377*) 1950 has reported studies on the

mechanism of erythropoietic stimulation in parabiotic rats during hypoxia. Chronic hypoxemia was induced in one partner of a pair of parabiotic rats by exposure to defined gas mixtures with low oxygen content. The other partner of the pair was kept in normal atmosphere throughout the experiment and showed normal values of the oxygen saturation of the blood. Erythropoiesis, estimated by the percentage of nucleated red cells in the bone marrow, showed a statistically significant stimulation in both animals. It was concluded, therefore, by the author that under these experimental conditions, the stimulus to erythropoiesis was not the partial pressure of oxygen in the bone marrow directly but a humoral factor elicited by hypoxemia in the one partner and transferred to the other one.

According to Tagliamonte (*380*) 1947, there is a reduction in corpuscular resistance in normal human subjects undergoing hypoxia by the rebreathing method. According to Penneys, Thomas, and Lewis (*376*) 1950, exposure of normal human subjects to low oxygen concentrations producing arterial oxygen saturations of 70 to 80 percent led to a significant drop in the eosinophil count. This effect was believed by the authors to indicate an increase of adrenal cortical activity following anoxemia. In one case the addition of carbon dioxide to the breathing mixture caused a slight rise in arterial oxygen saturation with a corresponding fall in the eosinophils while no change was observed in other subjects. In these experiments the total period of anoxemia ranged from 17 to 24 minutes.

In experimental animals, hypoxia may produce changes in plasma protein (*371, 372, 375*). Cordier and Coudier (*372*) found that dogs subjected to 7 percent oxygen showed an increase in plasma protein.

370. Berk, L., J. H. Burchenal, T. Wood, and W. B. Castle. Oxygen saturation of sternal marrow blood with special reference to pathogenesis of polycythemia vera. *Proc. Soc. exp. Biol., N. Y.*, 1948, *69:* 316–320. [P]

371. Cordier, D. and R. Coudier. Étude spectrale du sang au cours de l'anoxie progressive. Spectres d'absorption de l'hemoglobine dans les hématies et en solution après hemolyse. *C. R. Soc. Biol., Paris,* 1950, *144:* 844–847. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 656. Abstr.

372. Cordier, D. and R. Coudier. Étude spectrale du sang au cours de l'anoxie progressive. Spectres d'absorption du plasma dans l'ultra-violet. *C. R. Soc. Biol., Paris,* 1950, *144:* 1053–1055. [P]

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380. Tagliamonte, B. Comportamento del numero degli eritrociti e della resistenza globulare in soggetti sottoposti ad anossia con il metodo della ri-respirazione. *Riv. Med. aero., Roma,* 1947, *10:* 302–315. (Italian, English, French, Spanish, and German summaries.)

6. LYMPHATICS

Malmejac, Chardon, and Gross (*381*) 1948 have reported modifications in the production of lymph in the course of hypoxia in chloralosed dogs subjected to oxygen-nitrogen mixtures with an oxygen percentage from 4 to 10 percent. When the respiratory movements diminished after an initial rise, the lymphatic flow was found to be rapidly reduced. During hypoxic hyperventilation there was an immediate augmentation and discharge of lymph from the thoracic canal, but when this was interrupted the discharge of lymph was reduced. The authors considered that the influence of vasomotor reactions initiated by hypoxia, especially in the splanchnic area, are the principal cause of the reduction of the lymphatic flow. This action was considered to be produced by vasoconstriction or by the local action of epinephrine.

381. Malmejac, J., G. Chardon, and A. Gross. Modifications dans la production de la lymphe au cours de l'anoxie. Analyse des mécanismes efficients. *C. R. Soc. Biol., Paris,* 1948, *142:* 509–510. [P]

7. RESPIRATION

The effects of hypoxia upon respiration have been investigated by a large number of investigators. Some of these studies are reported in the references given in the following list. For recent descriptions of the actual respiratory responses to hypoxia, papers by the following should be consulted: Chambers, Brewer, Davenport, and Goldschmidt (*386*) 1947; Davenport, Brewer, Chambers, and Goldschmidt (*387*) 1947; Dripps and Comroe (*388*) 1948; Georges and Sonne (*394*) 1947; Gollwitzer-Meier (*395*) 1947; Houston (*401*) 1946; Korkes, Chinn,

and Marriott (*403*) 1948; Peyser, Sass-Kortsak, and Verzar (*406*) 1951; Sillani (*407*) 1947; and Smith (*408*) 1948.

Papers by the following may be consulted for investigations on the physiology of the respiratory center as affected by hypoxia; Bjurstedt (*384*) 1946; Ferro-Milone (*392*) 1951; Georg and Sonne (*393*) 1948–49; Grandpierre and Franck (*396*) 1950; Jaggi (*402*) 1950; and Weterings (*409*) 1948.

For papers offering hypotheses to explain the mechanisms of the effects of hypoxia on respiration, reports by the following authors may be consulted: Binet and Strumza (*382*) 1946; Fabinyi and Szebehely (*390*) 1949 and (*391*) 1950; Grandpierre, Franck, and Lemaire (*397*) 1949; Gray (*398*) 1946; and Lenggenhager (*404*) 1947.

382. **Binet, L. and M. U. Strumza.** Mécanisme de la persistance de l'activité nerveuse respiratoire dans l'anoxémie. *Méd. aeronaut.*, 1946, *1:* 338–340. [P]

383. **Binet, L. and M. V. Strumza.** Le taux de l'oxygène dans le sang artériel au début de l'apnée anoxique. *C. R. Soc. Biol., Paris,* 1949, *143:* 44. [P]

384. **Bjurstedt, A. G. H.** Interaction of centrogenic and chemoreflex control of breathing during oxygen deficiency at rest. *Acta physiol. scand.*, 1946, Supplementum. *38:* 88 pp. [R] [P]

385. **Brucer, M., G. L. Herman, and H. G. Swann.** Interrelationship of cardiorespiratory events in anoxia. *Amer. J. Physiol.*, 1950, *160:* 138–148. [M] [R]

386. **Chambers, A. H., G. Brewer, H. W. Davenport, and S. Goldschmidt.** The respiratory responses to anoxemia of the normal unanesthetized dog and their causes. *Amer. J. Physiol.*, 1947, *148:* 392–405. [P]

387. **Davenport, H. W., G. Brewer, A. H. Chambers, and S. Goldschmidt.** The respiratory responses to anoxemia of unanesthetized dogs with chronically denervated aortic and carotid chemoreceptors and their causes. *Amer. J. Physiol.*, 1947, *148:* 406–416. [P]

388. **Dripps, R. D. and J. H. Comroe, Jr.** The effect of inhalation of high and of low oxygen concentration upon human respiration and circulation. *Amer. J. med. Sci.*, 1947, 213/2: 248–294. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 174.

389. **Euler, U. S. and G. Liljestrand.** Observations on the pulmonary arterial blood pressure in the cat. *Acta physiol. scand.*, 1946, *12:* 301–320. [P]

390. **Fabinyi, M., and J. Szebehely.** Further investigations about the histamine hypothesis of the oxygen deficiency. *Arch. int. Pharmacodyn.*, 1949, *78:* 354–361. *Abstr. World Med.*, 1949, *6:* 264.

391. **Fabinyi, M. and J. Szebehely.** On the role of histamine in hyperpnoea caused by oxygen lack. *XVIII Intern. Physiol. Congr.*, 1950, 191–192.

392. **Ferro-milone, F.** Riglessi da impossia nella diminuita eccitabilita del centro respiratorio bulbare. *Boll. Soc. ital Biol. sper.*, 1951, *27:* 34–36. [P]

393. **Georg, J. and L. M. Sonne.** The relation of the oxygen tension of the inspiratory air to the chemoreceptor response during work. *Acta physiol. scand.*, 1948–49, *16:* 52–62. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 778. Abstr. [P]

394. **Georg, J and L. M. Sonne.** Undersøgelser over puls og respiration ved faldende ilttension i inspirationsluften. [An investigation of the effect of falling oxygen tension in the inspired air on pulse and respiration.] *Bibl. Laeger.*, 1947, *139:* 41–50. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 142. Abstr.

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396. **Grandpierre, R. and C. Franck.** Notions actuelles sur l'organisation et le fonctionnement des centres nerveux respiratoires. II. La régulation de la respiration. *Méd. aeronaut.*, 1950, *5:* 297–353. [P] [R]

397. **Grandpierre, R., C. Franck, and R. Lemaire.** Action de l'adrénaline sur le rythme respiratoire au cours de l'anoxémie hypocapnique. *C. R. Soc. Biol., Paris,* 1949, *143:* 1105–1107. [P]

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399. **Harris, A. S.** Inspiratory tonus in anoxia. *Amer. J. Physiol.*, 1945, *143:* 140–147.

400. **Hesse, R., E. Opitz, and F. Palme.** Darstellung der Höhenanpassung im Gebirge durch Sauerstoffmangel. I. Atmung und Alveolarluft bei Rückatmungsversuchen berschiedener Dauer. *Pflüg. Arch. ges Physiol.*, 1944, *248:* 283–297. [P]

401. **Houston, C. S.** The effect of pulmonary ventilation on anoxemia. *Amer. J. Physiol.*, 1946, *146:* 613–621. [P]

402. **Jaggi, F.** Über die Sensibilisierung des Atemzentrums durch den Sauerstoffmangel in der Höhe. *Méd. aeronaut.*, 1950, *5:* 97. (French abstract.) These (Med.) Berne, Langnau, Vogeli et Moser, Editeur. 1948. [P]

403. **Korkes, S., H. I. Chinn, and W. Marriott.** Oxygen consumption at low oxygen tensions. USAF. Randolph Field, Texas. School of aviation medicine, *Project 21–02–101, Rept. no. 1,* November 1948, 4 pp.

404. **Lenggenhager, K.** Worauf beruhen die Störungen bei Hyperventilation? Kritische Einwände gegen die herrschende theorie des Gasaustausches. *Helv. med. acta.*, 1947, *14:* 137–173. [P]

405. **Melik-Megrabov, A. M.** Iavleniia gipoksii narusheniiakh krovoobrashcheniia i dykhaniia razlichnoi etiologii. [The phenomenon of hypoxia in blood circulation and respiratory disorders of various etiology.] pp. 162–167 in: *Gipoksiia,* Kiev, Akad. Nauk. Ukr., 1949, 415 pp.

406. **Peyser, E., A. Saas-Kortsak, and F. Verzar.** Influence of O_2 content of inspired air on total lung volume. *Amer. J. Physiol.*, 1950, *163:* 111–117. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 760. Abstr.

407. **Sillani, L. S.** Comportamento della ventilazione polmonare in anossia. *Riv. med. aero., Roma,* 1947, *10:* 499–508. [P]

408. **Smith, R. E.** Physiological responses to hypoxia induced in man by inspiration of a low O_2–N_2 mixture. U. S. Navy. NMRI. *Project NM 001 003 X–313, Rept. no. 2,* 3 May 1948, 5 pp.

409. **Weterings, P. A. A.** The inhibitory effect of the oxygen pressure in blood on respiration through the intermediacy of chemo-receptors. *Acta med. scand.*, 1948, *130:* 232–258.

8. ALIMENTARY TRACT

The name of Van Liere has come to be associated with research upon the effects of low oxygen on the functions of the alimentary tract. In a recent paper, Van Liere, Stickney, and Northup (*412*) 1951 have examined the effects of anoxia on intestinal motility and on blood sugar in pups. Anoxic anoxia produced a signficant decrease in propulsive motility, but anemic anoxia had no significant effect. This is in direct contrast to the findings in adult dogs. The hyperglycemic response of pups to hypoxia was distinctly less than that of adult dogs. These findings are in conformity with those of Lemaire and Bouverot (*411*) 1949, who found in dogs a fall in intestinal tonus during anoxemia and adrenalin injection. The drop in tone was accompanied by a striking diminution of the amplitude of intestinal movements. In these experiments, the splanchnic nerves were sectioned and the movements of the intestine were noted during inhalation, for 2 minutes and 45 seconds, to a mixture containing 7 percent oxygen. Cordier and Chanel (*410*) 1949 subjected rats to oxygen percentages as low as 1 percent. Just before exposure there was introduced into the stomach 2 cu. cm. of glucose solution (5.4 percent to 50 percent). At oxygen concentrations of 12 to 21 percent, 99 percent of the glucose had passed into the intestine within an hour's time. In those rats breathing 5 percent oxygen, only 35 percent of the glucose passed into the intestine at the end of an hour. Cordier and Chanel (*419*) 1949 also pointed out that prolonged and severe hypoxia diminishes intestinal absorption of glucose in the rat. For a study of the effects of exposure of isolated rabbit's intestine to a mixture containing no oxygen, a paper by West, Hadden, and Farsh (*413*) 1951 may be consulted. Complete anoxia resulted in total mechanical inactivity in 3 to 5 minutes.

410. Cordier, D. and J. Chanel. Influence de la tension d'oxygène dans l'air inspiré sur la vitesse du transit gastrique chez le rat. *C. R. Soc. Biol., Paris,* 1949, *143:* 493–495. [P]

411. Lemaire, R. and P. Bouverot. Action de l'adrénaline sur l'intestin au cours de l'anoxémie hypocapnique. *C. R. Soc. Biol., Paris,* 1949, *143:* 1113–1115. [P]

412. Van Liere, E. J., J. C. Stickney, and D. W. Northup. Effect of anoxia on intestinal motility and on blood sugar in pups. *Amer. J. Physiol.,* 1951, *167:* 103–107. [P]

413. West, T. C., G. Hadden, and A. Farah. Effect of anoxia on response of the isolated intestine to various drugs and enzyme inhibitors. *Amer. J. Physiol.,* 1951, *164:* 565–572. [P]

9. METABOLISM

The effect of decrease of oxygen tension in the inspired air upon the rate of oxygen consumption has been investigated experimentally by Beyne, Boy, and Polonovski (*414*) 1946. These investigators concluded that with a decrease of oxygen tension there was also a decrease in oxygen consumption. The suppression of oxidation was accompanied by a decrease in body temperature and an accumulation in the body of products of incomplete oxidation. Other investigations reported in the physiological literature indicate a considerable variation in the oxygen consumption rate of man and animals during hypoxia. Both increases and decreases have been found. Hemingway and Nahas (*427*) 1951 carried out a series of observations using normal unanesthetized dogs breathing an 8 percent oxygen mixture. The oxygen consumption rate was first found to decrease and then to increase to a value exceeding the control value of air breathing. In a study of the effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men, Kety and Schmidt (*430*) 1948 found that inhalation of a 10-percent oxygen mixture resulted in an increase of cerebral blood flow, but no significant change in cerebral oxygen consumption.

Hypoxia results in a mobilization of blood sugar with a drainage on glycogen stores. For experimental studies on this phenomenon, papers by the following may be consulted: Cordier and Dessaux (*420*) 1949 and (*421*) 1951; Cordier and Touze (*422*) 1949; Leonardi (*432*) 1947; Leonardi (*433*) 1947; and Smith and Oster (*444*) 1946. The results of decrease in partial pressure of oxygen of the inspired air upon lactic-acid metabolism have been reported by Loeschicke and Loeschicke (*434*) 1947 and Lundin and Strom (*435*) 1947.

According to Sillani (*443*) 1948, exposure of human subjects to short-lasting periods of hypoxia results in a slight decrease of ketone bodies and total fats as well as lipoid phosphorus. In control tests under normal air conditions, these variations did not occur.

Regarding the effects of anoxic anoxia on bile secretion in the rat, MacLachlan, Sleeth, and Gover (*436*) 1947 found no significant difference in the amount of bile salts excreted by a bile fistula rat when exposed for 4-hour periods to decreased oxygen tension (63 mm. Hg and 53 mm. Hg). Chardon, Neverre, and Jeannoel (*418*) 1948 measured the bile flow in the cystic canal in chloralosed dogs subjected to 3 percent oxygen in nitrogen. At first there was an acceleration of bile flow. This was followed by a decrease of bile secretion. For studies on the metabolism of the liver and spleen under conditions of hypoxia, papers by Brin (*416*) 1949 and Rein (*442*) 1950 should be consulted.

Regarding the influence of hypoxia on pancreatic secretion, Chardon and Gross (*417*) 1946 found in dogs under chloralose anesthesia exposed to 2 to 5 percent oxygen that there was at first a considerable decrease in pancreatic secretion with return to normal values after the first 30 minutes.

Ivy, Farmer, Krasno, Freeman, Burrill, Bouthwell, Cilley, Scow, and Friedemann (*429*) 1945 reported a detailed study on the metabolic effects of mild hypoxia on human subjects. Eleven young subjects were exposed to a simulated altitude of 18,000 feet for 1 hour each day, 3 times a week for 9 weeks. The subjects were maintained on a complete diet containing 91 mg. of ascorbic acid daily. The exposure period was preceded by 5 weeks on the diet and followed by a post-exposure period of 3 weeks during which control determinations were made. Repeated exposure to altitude caused a decrease in the daily urinary excretion of viamin C from an average of 33.6 mg. to 0.12 mg. The plasma level of ascorbic acid decreased from an average control level from 0.73 mg. percent to 0.58 mg. percent during the last 3 weeks of exposure. Repeated exposure to a simulated altitude of 18,000 feet without supplementary oxygen did not affect the urinary output of thiamin, riboflavin, and alpha-ketoglutaric acid, pyruvic acid, and acetone bodies. There was no clearly significant change in the sedimentation rate of the erythrocytes or in the hematocrit determinations. Glucose tolerance was not decidely changed. Depletion of ascorbic acid was considered to be due to increased utilization. Exposure to a simulated altitude of 18,000 feet without added oxygen caused a temporary increase in the excretion of sodium, potassium, and chloride. The excretion of 17-ketosteroids decreased for the first 6 weeks, but during the last 3 weeks tended to return to the control level but did not quite reach it. The excretion of ascorbic acid, amino nitrogen, and 17-ketosteroids tended to be parallel when subjects were repeatedly exposed to 18,000 feet without supplementary oxygen. Exposure of subjects to a simulated altitude of 35,000 feet with oxygen inhalation resulted in hypersecretion of these substances.

Crossed circulation studies on dogs reported by Malmejac and Chardon (*437*) 1946, (*438*) 1947, and (*439*) 1950 indicate that hypoxia produced by inhalation of gas mixtures containing 6 to 10 percent oxygen results in increased secretion of epinephrine. According to Grandpierre, Franck, and Lemaire (*426*) 1948, exposure to a 14-percent oxygen mixture causes a diminution of the efficacy of epinephrine in producing hypertensive and hyperglycemic reactions. Van Loo, Surtshin, and Katz (*445*) 1948 have investigated the role of the adrenal glands in hypoxia. In unilaterally adrenalectomized animals they found that diversion into a syringe of the venous blood draining from the remaining adrenal gland resulted in no significant change in the hypoxemic pressor response, but diminished considerably the posthypoxemic pressor response. Blood collected from the phase of falling blood pressure during nitrogen breathing had more pressor activity than that collected during the earlier phases of hypoxemia. Reinjection of such collected blood immediately after the peak of the posthypoxemia response caused the pressure to rise to a level similar to that attained in the controls. The authors concluded that the adrenal gland plays only a small part in the production of the arterial pressor response after reaeration. Pressor substances liberated from the adrenal gland during severe hypoxemia do not exert pressor effects until the tissues are reoxygenated.

For a study of the metabolic changes in muscle produced by oxygen lack, a paper by Endo (*423*) 1944 may be consulted. This paper contains a number of references. Kottke, Phalen, Taylor, Visscher, and Evans (*431*) 1948 have studied the effect of hypoxia upon temperature regulation of mice, dogs, and man. Hypoxia was found under the conditions of these experiments to decrease the capacity of both the animals and human subjects to control body temperature during exposure to cold. Loss of temperature control and fall in body temperature was most striking in the mouse and least marked in man. Hypoxia was found to inhibit shivering in all three species studied. Hypoxia in man was also shown to result in a greater dissipation of heat from the skin in the cold environment. Decreased environmental and body temperature favored the survival of mice exposed to progressive hypoxia. Between 20° to 37° C. the survival was increased by approximately 1,000 feet per 1° C. drop in temperature. This striking protection against death at altitude afforded by drop in body in temperature of mice would seem to be due to decreased oxygen demand at lower body temperatures and parallels the increased altitude tolerance of thyroidectomized animals. Goebel, Fukas, Klante, and Imdahl (*425*) 1951 subjected rats to 20-hour sessions in an atmosphere containing 7 percent oxygen in nitrogen. Oxygen consumption fell soon after exposure, and after 20 hours was only 50 percent of the normal value. The body temperature was observed to decrease quickly after exposure. At the end of the experiment the temperature rapidly climbed to normal. Oxygen consumption and body temperature reached control valves, at the same time, in about 6 hours.

For further studies on the effects of hypoxia upon metabolism, papers by the following authors may be consulted: Bollman, Fazio, and Faulconer (*415*) 1951; Fabinyi and Szebehelyi (*424*) 1948; Herber (*428*) 1948; Moon (*440*) 1950; and Parkes (*441*) 1951.

414. Beyne, J., G. Boy, and M. Polonovski. Le métabolism de l'oxygène au cours de l'anoxie. *Méd. aeronaut.*, 1946, *1:* 131–145. [D] [R]

415. Bollman, J. L., A. N. Fazio, and A. Faulconer, Jr. Some factors influencing the effects of anoxic anoxia. *Anesthesiol.*, 1951, *12:* 420–430 and 441.

416. Brin, B. M. Izmenenie intensivnosti okisleniia pri gipoksii pecheny (fistula Ekka). [Changes in oxidation intensivity in liver hypoxia.] [Eck fistula.] pp. 205–209 in: *Gipoksiia,* Kiev, Akad. Nauk. Ukr. SSR., 1949, 415 pp.

417. Chardon, G. and A. Gross. Influence de l'anoxie sur la sécrétion pancréatique externe. *C. R. Soc. Biol., Paris,* 1946, *140:* 1004. [P]

418. Chardon, G., G. Neverre, and G. Jeannoel. Modifications de la sécrétion biliaire sous l'influence du déficit en oxygène. *C. R. Soc. Biol., Paris,* 1948, *143:* 697–698. [P]

419. Cordier, D. and J. Chanel. Influence de la tension d'oxygène dans l'air inspiré sur la vitesse de l'absorption intestinale des solutions de glucose chez le rat. *J. Physiol., Paris,* 1949, *41:* 151–154A. [P]

420. Cordier, D. and G. Dessaux. Modifications du taux du glycogène cardiaque chez le rat sous l'influence de l'anoxie et du choc traumatique. *J. Physiol., Paris,* 1949, *41:* 159A–161A. [P]

421. Cordier, D. and G. Dessaux. Modifications du taux du glycogène cardiaque sous l'influence de l'anoxie, de l'asphyxie et de l'intoxication carbonique rapides. *C. R. Soc. Biol., Paris,* 1951, *145:* 727–729.

422. Cordier, D. and M. Touze. Modifications réversibles de la phosphorolyse hépatique du glycogène sous l'influence de l'anoxie anoxique chez le rat. *C. R. Soc. Biol., Paris,* 1949, *143:* 1060–1063. [P]

423. Endo, K. Über die Veränderungen der Stoffumsätze des Muskels in der Ruhe und bei der Arbeit im O_2—Mangel. *Tôhoku J. exp. Med.*, 1944, *47:* 195–222. [P]

424. Fabinyi, M. and J. Szebehelyi. The role of histamine in the symptoms caused by decreased partial pressure of oxygen. *Arch. int. Pharmacodyn.*, 1948, *76:* 397–416. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 254. Abstr. [P]

425. Goebel, A., H. K. Fukas, W. Klante, and H. Imdahl. Sauerstoffverbrauch und Körpertemperatur von Ratten im Sauerstoffmangel. *Z. ges. exp. Med.*, 1951, *117:* 384–392.

426. Grandpierre, R., C. Franck, and R. Lemaire. Influence des variations du taux des gaz respiratoires sur l'efficacité de l'adrénaline. *Méd. aeronaut.*, 1948, *3:* 227–229. [P]

427. Hemingway, A. and G. G. Mahas. Oxygen consumption rate during hypoxia. *Amer. J. Physiol.*, 1951, *167:* 794. Abstr.

428. Herber, F. J. Metabolic changes of blood and tissue gases during asphyxia. *Amer. J. Physiol.*, 1948, *152:* 687–695. [P]

429. Ivy, A. C., C. J. Farmer, L. R. Krasno, S. Freeman, M. W. Burrill, J. H. Boutwell, J. H. Cilley, J. Scow, and T. E. Friedemann. The effect on human subjects of the degree of ascorbic acid deficiency induced and of the disturbance of the metabolism of the vitamin by mild anoxia and its correlation with acid-base disturbances and 17-ketosteroid excretion. U. S. NRC–CAM. *OEMcmr-236, C. A. M. rept. no. 457,* 30 June 1945, 4 pp. [P]

430. Kety, S. S. and C. F. Schmidt. The effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young men. *J. clin. Invest.*, 1948, *27:* 484–492. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 488–489. [P]

431. Kottke, F. J., J. S. Phalen, C. B. Taylor, M. B. Visscher, and G. T. Evans. Effect of hypoxia upon temperature regulation of mice, dogs, and man. *Amer. J. Physiol.*, 1948, *153:* 10–15. [P]

432. Leonardi, G. Iperalcolemia endogena in condizioni di anossia. *Boll. Soc. ital. Biol. sper.*, 1947, *23:* 477–480. [P]

433. Leonardi, G. Iperalcolemia endogena nell'uomo in condizioni di ipossia sperimentale. *Boll. Soc. ital. Biol. sper.*, 1947, *23:* 703–705.

434. Loeschicke, G. and H. H. Loeschicke. Über den Milchsäureaustausch zwischen arteriellem Blut und Gehirngewebe und seine Veränderungen im Sauerstoffmangel. *Pflüg. Arch. ges. Physiol.*, 1947, *249:* 521–538. [P]

435. Lundin, G. and G. Strom. The concentration of blood lactic acid in man during muscular work in relation to the partial pressure of oxygen of the inspired air. *Acta physiol. scand.*, 1947, *13:* 253–266.

436. MacLachlan, P. L., D. K. Sleeth, and J. Gover. Effect of anoxic anoxia on bile secretion in the rat. *Proc. Soc. exp. Biol., N. Y.*, 1947, *66:* 275–276 [P]

437. Malmejac, J. and G. Chardon. Sur la résistance du système adrénalino-sécréteur à l'anoxie. *C. R. Soc. Biol., Paris,* 1946, *140:* 1005–1006. [P]

438. Malmejac, J. and G. Chardon. Mécanisme de déclenchement et d'entretien de la sécrétion surrénale d'arenaline en anoxie. *C. R. Soc. Biol., Paris,* 1947, *141:* 395–396. [P]

439. Malmejac, J. and G. Chardon. Influence du déficit en oxygène sur l'adrénalino-sécrétion. *Méd. aeronaut.*, 1950, *5:* 19–30.

440. Moon, V. H. Symposium on inhalational therapy. The origins and effects of anoxia. *Bull. N. Y. Acad. Med.*, 1950, *26:* 361–370.

441. Parkes, A. S. Some factors affecting resistance to anoxia in mice. *J. Endocrin.*, October 1951, *7:* LXII. [P]

442. Rein, F. H. Die Funktion von Milz und Leber zur Ertragung von lokalem und allgemeinem Sauerstoff-Mangel. *XVIII Intern. physiol, Congr.*, 1950, 409. [D]

443. Sillani, L. S. Comportamento dei grassi totali, del fostoro lipoideo, e dei corpi chetonici nel sangue dell organismo umano sottoposto all azione di prolungata anossia. *Riv. Med. aero., Roma,* 1948, *11:* 15–24. (English, French, Spanish, and German summaries.) [P]

444. Smith, D. C. and R. H. Oster. Influence of blood sugar levels on resistance to low oxygen tension in the cat. *Amer. J. Physiol.*, 1946, *146:* 26–32. [P]

445. Van Loo, A., A. Surtshin, and L. N. Katz. Nature of the two pressor responses to acute hypoxemia with some observations on the role of the adrenals in hypoxia. *Amer. J. Physiol.*, 1948, *154:* 397–404. [P]

10. TEMPERATURE

Tolerance to reduced oxygen tensions is known to be greater in new-born animals. Adolph (*446*) 1948 found that rats between 1 and 4 days of age showed a greater tolerance to complete anoxia than

those 11 days old or older. As indicated by a report of Miller, Miller, and Farrar (*447*) 1951, guinea pigs showed an increased resistance to asphyxia if moderately cooled. The time of death of 202 asphyxiated, neonatal animals was recorded at colonic temperatures between 45.2° C. and 10.9° C. Death from temperature occurred at colonic levels above 44°C. and below 19° C. A linear increase in survival of approximately 50 percent per 10° C. decrease in temperature was recorded for the entire nonlethal temperature range. The shortest anoxic survival was 81 seconds at 44.2° C., the longest was at 617 seconds at 14° C. One hundred and three young adults similarly tested showed a linear increase of 35 percent per each 10° C. decrease in temperature. In the adult animals, deaths occurred above 44° C. and below 16° C.

446. Adolph, E. F. Loss of tolerances to cold and to anoxia in infant rats. *Anat. Rec.*, 1948, *101:* 737, Abstr. [P]

447. Miller, J. A., Jr., F. S. Miller, and C. B. Farrar. Effects of temperature upon resistance of guinea pigs to anoxia. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 92.

11. KIDNEY

Franklin, McGee, and Ullman (*451*) 1951 in observations on rabbits reported a diversion of the renal cortical blood flow following intense anoxia and hypercapnia. Urine flow was also inhibited. These renal and urinary changes were not seen after denervation of the renal pedicle. The blood-flow changes in the kidney were independent of the blood pressure and may have depended, according to the authors, upon chemosensitive centers in the spinal cord. Malmejac, Chardon, and Gross (*453*) 1946 observed intense vasoconstriction at the beginning of 8 percent oxygen inhalation, but secondarily the hypoxia was not sufficient to evoke a change in urinary output. Similar findings have been reported by Brull and Divry (*449*) 1951. With Brull's mechanical heart technique, the kidneys of dogs were perfused alternately with arterial and venous blood under varying pressures. It was found that under normal conditions of flow the oxygen requirements of the kidney could be completely covered by an oxygen content of only 30 percent of normal. A decrease of the inflow pressure to 50 mm. Hg or lower caused a decrease in venous outflow, a cessation of secretion, and a decrease of oxygen consumption to 70 percent of normal. It was concluded by the authors that a decrease of blood flow through the kidney is practically the only mechanism capable of stopping secretion. Hypoxia itself was considered to be without effect.

Berger, Galdston, and Horwitz (*448, 452*) 1949 have investigated the effect of hypoxia upon human renal function. In these experiments, human subjects with normal cardiovascular and respiratory systems inhaled air mixtures containing 14 percent oxygen. This degree of hypoxia in the normal subjects resulted in barely perceptible changes in circulatory and respiratory dynamics. Similar studies were conducted on two emphysematous subjects with arterial blood oxygen tensions of approximately 50 mm. Hg while breathing room air and, again, while breathing 100 percent oxygen. For the emphysematous subjects the periods of breathing room air were considered as the hypoxic periods. In both the normal and emphysematous subjects, studies were made of glomerular filtration rate, inulin clearance, renal plasma flow, and para-aminohippurate clearance. The urine was collected in 15- to 30-minute periods by catheter. Urine pH was measured. Blood was drawn from the femoral artery. The average pulse rate did not change significantly in 4 subjects, while in 5 others it rose 8 to 14 beats per minute during the anoxic periods. Only in 1 instance did the blood pressure rise as much as 13 mm. Hg. Renal plasma flow remained the same or tended to increase during hypoxia in all normal subjects. In the two subjects with pulmonary emphysema, the administration of 100 percent oxygen induced a fall in renal plasma flow. In these subjects the period of breathing room air was associated with an increase in renal plasma flow of 29 percent. The filtration rate did not change during hypoxia in four cases. There was an increase of 9 to 23 percent in 4 cases, and a decrease of 19 percent in 1. The most pronounced effect of hypoxia on renal function was an invariable and frequently marked increase in the rate of excretion of sodium, chloride, and water. Urine flow tended to increase during the hypoxic periods. Urinary pH shifted to higher values in all subjects except one. Ammonia production decreased in all but one observation. Potassium was increased. Proteinuria did not develop. The authors drew the conclusion that hypoxia alone does not appear to result in reduction of renal plasma flow or retention of salt and water. In similar studies on two normal young male subjects carried out by Caldwell, Rolf, and White (*450*) in 1949, it was determined that breathing low oxygen mixtures at atmospheric pressure, the oxygen percentage being 9.3 percent, for periods of a few minutes produced no effect on para-aminohippurate or inulin clearance. In these normal subjects there was no effect on renal vascular resistance or plasma glucose levels.

448. Berger, E. Y., M. Galdston, and S. A. Horwitz. The effect of anoxic anoxia on the human kidney. *J. clin. Invest.*, 1949, *28:* 648–651. [P]

449. Brull, L. and A. Divry. Metabolic and secretory activity of the kidney under anoxemia. *Arch. int. Physiol.*, 1951, *58:* 415–423.

450. Caldwell, F. T., D. Rolf, and H. L. White. Effects of acute hypoxia on renal circulation in man. *J. appl. Physiol.*, 1949, *1:* 597–600. [P]

451. Franklin, K. J., L. E. McGee, and E. Ullman. Effects of severe asphyxia on the kidney and urine flow. *J. Physiol.*, 1951, *112:* 43–53. [P]

452. Galdston, M., E. Y. Berger, and S. A. Horwitz. The effect of anoxic anoxia on the human kidney. *J. clin. Invest.*, 1949, *28:* 648–652.

453. Malmejac, J., G. Shardon, and A. Gross. Influence de l'anoxie sur la sécrétion urinaire. *C. R. Soc. Biol., Paris*, 1946, *140:* 1000–1002. [P]

12. EFFECTS OF CARBON DIOXIDE ON HYPOXIA

For studies on the effects of carbon dioxide administration in oxygen mixtures on the hypoxic subject and the effect of adding carbon dioxide to inspired oxygen on tolerance to hypoxia, papers by the following should be consulted: Adler (*454*) 1947; Binet and Strumza (*455*) 1950; Ivy, Grodins, Adler, and Snapp (*456, 457*) 1947; Otis, Rahn, and Chadwick (*458*) 1949; Smith (*459*) 1950; and Stone, Webster, Kopala, and Gurdjian (*460*) 1946.

Studies on the effects of carbon dioxide inhalation on the hypoxic animal carried out by Ivy, Grodins, Adler, and Snapp (*456, 457*) 1947 consisted of tests of the respiratory and circulatory responses to carbon dioxide (5 percent, 6 percent, and 15 percent) in dogs during the course of acute, severe hypoxia produced by the inhalation of 4 percent oxygen. Under these conditions the stimulatory effects of carbon dioxide progressively decreased, soon disappeared, and were finally reversed. Fifteen percent carbon dioxide produced more frequent and more profound respiratory and circulatory depression than did 5 percent carbon dioxide. Five percent carbon dioxide given at the beginning of collapse had no demonstrable effect on blood pressure or respiration. Adler (*454*) 1947 has concluded that under conditions of severe hypoxia in dogs, carbon dioxide is not indicated as an inhalant in gas mixtures used for resuscitation since it not only fails to stimulate the respiratory center and the peripheral chemoreceptors but also in the presence of severe hypoxia a 5 percent carbon dioxide concentration may act as a respiratory and circulatory depressant. The depressing effects of a 15-percent concentration are even more striking. In confirmation of experimental findings, the recent literature emphasizes the potential hazard of use of carbon dioxide in oxygen for purposes of resuscitation.

Although there is evidence in the literature that carbon dioxide may under certain circumstances increase tolerance to hypoxia (see, for example, *459* and *460*), nevertheless it does not appear that addition of carbon dioxide to respiratory mixtures is a practicable or effective means of improving efficiency under conditions of hypoxia. For an additional report on this subject, a paper by Otis, Rahn, and Chadwick (*458*) 1949 may be consulted.

454. Adler, H. F. Effect of carbon dioxide on an anoxic animal. USAF. Randolph Field, Texas. School of aviation medicine. *Project 474, Rept. no. 2,* 31 March 1947, 1 p. [P]

455. Binet, L. and M. V. Strumza. Variations du taux du CO_2 total du plasma artériel et résistance des centres respiratoires à l'anoxie. *J. Physiol., Paris,* 1950, *42:* 249–258. [P]

456. Ivy, J. H., F. S. Grodins, H. F. Adler, and F. E. Snapp. Studies on asphyxia. II. Effects of carbon dioxide inhalation on an anoxic animal. *J. Aviat. Med.*, 1947, *18:* 577–589. [P]

457. Ivy, J. H., F. S. Grodins, H. F. Adler, and F. E. Snapp. Studies on asphyxia. II. Effects of carbon dioxide inhalation on an anoxic animal. U. S. AAF. Randolph Field, Texas, School of aviation medicine, *Project 474, Rept. no. 2,* 17 July 1947, 5 pp. [P]

458. Otis, A. B., H. Rahn, and L. E. Chadwick. Effects of adding carbon dioxide to inspired oxygen on tolerance to high altitudes. *Proc. Soc. exp. Biol., N. Y.*, 1949, *70:* 487–490.

459. Smith, R. E. Effects of carbon dioxide inhalation upon the hypoxia response of normal men. *XVIII Intern. physiol. Congr.*, 1950, 457.

460. Stone, W. E., J. E. Webster, J. Kopala, and E. S. Gurdjian. Effects of carbon dioxide administration on cerebral metabolism in hypoxia. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 101.

13. TOLERANCE

For studies on the effects of various factors on sensitivity to hypoxia, papers by the following should be consulted: Dustin (*461*) 1949; Miller, Miller, and Farrar (*462*) 1951; Smith and Smith (*463*) 1951; and Snapp, Adler, and Kramer (*464*) 1948. According to Dustin (*461*) 1949, adrenolytic drugs were ineffective in increasing the susceptibility of anesthetized dogs to hypoxia. According to Snapp, Adler, and Kramer (*464*) 1948, alphalobeline and coramine were not effective in stimulating lightly nembutalized dogs rendered apneic by breathing pure nitrogen. Metrazol caused spontaneous respiration in 2 out of 9 dogs injected. Amphetamine sulfate caused spontaneous respiration in 10 out of 18 dogs. Intravenous injection of glucose before hypoxia did not increase the resistance of the animal to oxygen lack. Artificial respiration with 100 percent oxygen was more effective in resuscitation than any of the drugs used. Miller, Miller, and Farrar (*462*) 1951 have shown experimentally in guinea pigs that each degree of tem-

perature reduction increases resistance to asphyxia until cold itself become lethal. In contrast, it is well known that increasing basal metabolic rate enhances the sensitivity of both man and animals to hypoxia. For example, Smith and Smith (*463*) 1951 have reported increased sensitivity to progressive hypoxia in thyroid-treated mice showing increased basal oxygen consumption. There was also decreased tolerance to exercise in these same animals. Thyroid administration superimposed upon radiation resulted in no increase in basal oxygen consumption beyond that caused by thyroid alone. However, resistance to progressive hypoxia was greater than with thyroid alone in these cases.

461. Dustin, E. H. Effects of hypoxia on respiration after adrenolytic drugs. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command, Aero medical laboratory. *Memo. rept. serial no. MCREXD-696-79H,* 10 February 949, 66 pp. [P]

462. Miller, J. A., Jr., F. S. Miller, and C. B. Farrar. Effects of temperature upon resistance of guinea pigs to anoxia. *Fed. Proc. Amer. Soc. exp. Biol.,* 1951, *10:* 92.

463. Smith, W. W. and F. Smith. Effects of thyroid and irradiation on sensitivity to hypoxia, basal rate of oxygen consumption and tolerance to exercise. *Amer. J. Physiol.,* 1951, *165:* 651–661.

464. Snapp, F. E., H. F. Adler, and K. Kramer. The effect of various respiratory stimulants on dogs depressed by anoxia. UASF. Randolph Field, Texas. School of aviation medicine, *Project 21-02-034, Rept. no. 1,* November 1948, 6 pp. [P]

B. LOW OXYGEN TENSIONS DUE TO DECOMPRESSION

1. GENERAL STUDIES

The references cited in this section provide access to the general subject of hypoxia due to decompression in aircraft or in decompression chambers or in mountain climbing. This subject is included in this Sourcebook because problems of hypoxia are encountered in submarine operations and will become more and more significant under conditions of submarine operations involving prolonged submergence. For discussions of the literature on hypoxia, reference may be made to annual review articles by Hoff and Fulton (*473*) 1947 and Hoff (*474*) 1948, (*475*) 1949, and (*476*) 1950. These reviews contain comprehensive bibliographies. Excellent reviews on hypoxia in man and animals by Fulton and Nims (*471*) 1941–46 and Nims (*480*) 1948 should be read. These serve as a useful guide to studies on the physiology of low oxygen tensions. A good review article coming from Italy is that of Vacca (*482*) 1949. This article covers research on hypoxia carried out between 1945 and 1948 and contains approximately 200 references on the subject as it applies to respiration, heart and circulation, nervous system, and metabolism.

465. Balanina, N. V. K voprosu o reaktivnosti organizma i o sostoianii aktivino soedinitel'noi tkani pri gipoksemii. [Reactivity of the organism and the condition of active connective tissue in hypoxemia.] *Arkhiv patol., Moskva,* 1947, *4:* 86–90.

466. Barach, A. L. Additional studies on anoxia and its treatment. pp. 43–85 in: *Physiologic therapy in respiratory diseases.* Second edition. Philadelphia, J. B. Lippincott Company, 1948, 408 pp.

467. Bartley, S. H. and E. Chute. Anoxia and related living conditions. pp. 71–90 in: *Fatigue and impairment in man.* New York, McGraw-Hill Book Co., Inc. 1947, 429 pp. [R] [P]

468. Binet, L. and M. V. Strumza. Effets de l'apnée anoxique prolongée et repetée. *C. R. Acad. Sci., Paris,* 1949, *229:* 688–690. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1494.

469. Castaigne, P. Les anoxies. *Pr. méd.,* 1950, *58:* 120–123. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1050.

470. Evrard, E. Observations expérimentales relatives aux effets des vitesses ascensionnelles rapides sur l'organisme de l'aviateur. (A suivre.) *Brux. méd.,* 1949, *29:* 3639–3657. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1003.

471. Fulton, J. F. and L. F. Nims. Decompression sickness. Anoxia in man and animals. Anoxia in man. pp. 11–14 in Final Rept. in: *Studies in Aviation Medicine.* Yale University School of Medicine, New Haven, Conn., Yale aero-medical research unit. 1941–1946. [P]

472. Gray, J. S. and F. S. Grodins. Respiration. Respiratory disturbances. *Annu. Rev. Physiol.,* 1951, *13:* 227–229. [R]

473. Hoff, E. C. and J. F. Fulton. Aviation medicine. pp. 261–285 in: *The cyclopedia of medicine, surgery, and specialties.* Edited by G. M. Piersol and E. L. Bortz. Philadelphia, F. A. Davis Co., 1947, pp. 1153. [R]

474. Hoff, E. C. Aviation medicine. pp. 229–252 in: *The cyclopedia of medicine, surgery, and specialties.* Edited by G. M. Piersol and E. L. Bortz. Philadelphia, F. A. Davis Co., 1948, 953 pp. [R]

475. Hoff, E. C. Aviation medicine. pp. 227–249 in: *The cyclopedia of medicine, surgery, and specialties.* Edited by G. M. Piersol and E. L. Bortz. Philadelphia, F. A. Davis Co., 1949, 989 pp. [R]

476. Hoff, E. C. Aviation medicine. pp. 229–256 in: *The cyclopedia of medicine, surgery, and specialties.* Edited by G. M. Piersol and E. L. Bortz. Philadelphia, F. A. Davis Co., 1950, 1021 pp. [R]

477. Ivy, A. C. High altitude problems in aviation. *Fed. Proc. Amer. Soc. exp. Biol.,* 1946, *5:* 319–327.

478. Lund, D. W. Altitude sickness, acute and chronic. pp. 4–378—4–384 in: *Treatment in general medicine.* Volume 4. Edited by Hobart A. Reimann. Fourth edition. Philadelphia, F. A. Davis Co., 1948, 776 pp.

479. Muralt, A. V. Klimaphysiologische Untersuchungen in der Schweiz. *Helvet. physiol. pharm. Acta.,* (*suppl.*), 1944, *3:* 7–14. [D]

480. Nims, L. F. Anoxia in aviation. *Annu. Rev. Physiol.,* 1948, *10:* 305–314. [R]

481. Tufts College. Altitude. 15 pp. in: Handbook of human engineering data for design engineers. Tufts College, Institute for applied experimental psychology. *SDC Human Engineering Project 20-G-1, Project Designation NR-783-001, Technical Report 199-1-1,* 1 December 1949, 410 pp.

482. Vacca, C. Risultati di moderne ricerche sugli effetti provocati dall'anossia nell'organismo umano. *Riv. Med. aero., Roma,* 1949, *12:* 59–92. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 762. [R]

483. Von Tavel, F. The influence of oxygen-lack on the human organism on brief exposure to high altitudes. A contribution to the question of functional capacity during flight at high altitude. *Helvet. physiol. pharm. Acta,* (*Supplementum*) 1943, *1:* 1–128. [P]

484. White, M. S. Prolonged hypoxia in aircraft passengers. The effects of a flight around the world in 6¼ days. *J. Aviat. Med.,* 1947, *18:* 244–251 and 288. [P]

2. SPECIAL SENSES

The use of flicker frequency, dotting, and writing tests in untrained subjects as a measure of response to hypoxia, has been critically tested by Murray (*498*) 1943. Results suggest that none of the tests are to be confidently recommended for selection of the individual with respect to response to hypoxia. However, the flicker test might prove useful in preliminary testing of a group. In experiments of Birren, Fisher, Vollmer, and King (*485*) 1946, critical flicker frequency and perimetry were used to determine changes in performance of small groups of subjects under hypoxic conditions, simulating altitudes of 10,000 feet and above. Body sway was used to demonstrate differences in performance at simulated altitudes of 14,000 feet and above. The magnitude of most changes were such that individual scores were within normal distribution of values at sea level and so could not be used as criteria, in a clinical sense, of extent of hypoxia in the individual. Perimetry and critical flicker frequency were not significantly altered. Apparently visual functions do not reflect factors determining imminent collapse of a subject to hypoxia. According to the authors, lack of correlation between performance decrements and these tests suggests considerable variation in the underlying physiological adjustments to hypoxia.

According to Motokawa and Iwama (*497*) 1949, the electric excitability of the human eye is a sensitive and accurate measure for oxygen deficiency and more suitable as an index of oxygen deficiency than light sensitivity.

Visual contrast discrimination has been used as a method of demonstrating the effect of hypoxia on sensory performance. Hecht, Hendley, and Frank (*494*) 1943 have studied visual-contrast discrimination in oxygen concentrations corresponding to altitudes up to 17,000 feet at 3 brightness levels corresponding to visual conditions between dawn and sunrise, between sunset and dark, and daytime conditions only. At these brightnesses, contrast discrimination was found to deteriorate at fairly low altitudes. The deterioration was obvious at 8,000 feet simulated altitude and became striking at a simulated altitude of 15,000 feet where, at low brightness, it was found that the contrast must be increased 100 percent over sea level before it can be recognized. The impairment of contrast recognition with increase in altitude was found to be greater at higher altitudes than lower. The impairment of contrast discrimination was found to vary inversely with brightness. It was found to be most evident under the lowest light intensities studied, but it was observed in all light intensities examined. The thresholds for night vision and day vision were equally affected by hypoxia. The authors recommended that even at moderate altitudes, say 8,000 feet, extra oxygen be taken at all illuminations except during full daylight. For further studies on contrast sensitivity, papers by Chapanis (*486*) 1946 and Peckham (*499*) 1943 may be consulted.

Regarding other effects of hypoxia upon visual function, Duquet (*487*) 1947 found that stereoscopic vision is quite resistant to hypoxia. In subjects exposed to 6,000 meters altitude, there was no appreciable difference between the values of stereoscopic parallax at altitude and sea level. In contrast, fatigue rate of accommodation and convergence are stated by Giardini (*491*) 1949 to be adversely affected at an altitude of 3,900 meters.

For studies on the effects of hypoxia on visual field, papers by the following may be consulted: Duguet and Bailliart (*488*) 1947, Halstead (*493*) 1945, Livingston (*495*) undated, and Posternak (*501*) 1948. For effects on night vision, papers by Maynard (*496*) 1945 and Posternak (*500*) 1948 should be read. According to Grandjean and Zwahlen (*492*) 1948, there was a rise in retinal arterial pressure in human subjects during a stay at the Jungfraujoch (3,450 meters). This elevation of pressure was considered by the authors to reflect a circulatory modification parallel to the level of the cerebral vessels. In a study by Duguet, Dumont, and Bailliard (*489*) 1947, young male subjects were submitted to simulated altitudes in a decompression chamber while changes in retinal vessels were continually studied by photographing the retina, first at ground level and then at 4,000, 5,000, and 6,000 meters. Experiments were first carried out without additional oxygen and then during administration of oxygen. Dilatation of the retinal vessels became noticeable and could be measured in photographs beginning at 4,000 meters. The dilatation increased with altitude, reaching its maximum at 6,000 meters, but did not increase after the subject had been at that level for 15 minutes. The magni-

tude of the dilatation varied from one subject to another, ranging from 10 to 39 percent of the diameter as measured at sea level. The average change was 21 percent. There was also venous dilatation ranging from 10 to 34 percent (average 18 percent) of the sea-level values. The retinal vessels were found to return to their original size immediately on return to sea level or while breathing oxygen at high altitudes. Hypoxic dilation of the retinal vessels was seen to be a test of circulatory efficiency.

For other studies on the effects of hypoxia upon visual function, papers by Ferrata (*490*) 1950, Scobee (*502*) 1944, and Tschirren and Wiesinger (*504*) 1948 should be consulted.

According to studies of Seitz and Smith (*503*) 1942, exposure of human subjects to a simulated altitude of 18,500 feet resulted in a decrement of auditory sensitivity as measured by speech intelligibility. As to tactile sensitivity, this was found to be increased by Awahlen and Grandjean (*505*) 1948 in subjects studied in the course of an expedition to Jungfraujoch (3,450 meters).

485. Birren, J. E., M. B. Fisher, E. Vollmer, and B. G. King. Effects of anoxia on performance at several simulated altitudes. *J. exp. Psychol.,* 1946, *36:* 35–49.

486. Chapanis, A. A device for demonstrating the effects of anoxia on vision. *J. Aviat. Med.* 1946, *17:* 348–356.

487. Duguet, J. Le comportement de la parallaxe stéréoscopique en anoxémie. *Méd. aeronaut.,* 1947, *2:* 36–42. [Ch] [P]

488 Duguet, J. and J. P. Bailliart. Les modifications du champ visuel central sous l'influence de l'anoxémie et de l'inhalation d'oxygène. *Méd. aeronaut.,* 1947, *2:* 516–523. [P] [D]

489. Duguet, J., P. Dumont, and J. P. Bailliart. The effects of anoxia on retinal vessels and retinal arterial pressure. *J. Aviat. Med.,* 1947, *18:* 516–520. [P]

490. Ferrata, L. Sul comportamento degli angioscotomi retinici in anossia. *Riv. Med. aero., Roma,* 1950, *13:* 50–56. (English, French, Spanish, and German summaries.)

491. Giardini, A. Faticabilità del meccanismo accomodazione-convergenza in anossia acuta. *Riv. Med. aero., Roma,* 1949, *12:* 511–525. (English, French, Spanish, and German summaries.) [P]

492. Grandjean, E. and P. Zwahlen. Modifications de l'ophtalmotonus et de la pression artérielle rétinienne en haute montagne. *Helvet. physiol. pharm. Acta,* 1948, *6:* 560–566. (English summary.)

493. Halstead, W. C. Chronic intermittent anoxia and impairment of peripheral vision. *Science,* 1945, *101:* 615–616. [P]

494. Hecht, S., C. D. Hendley, and S. Frank. The effect of anoxia on visual contrast discrimination. U. S. NRC–CAM. *C. A. M. rept. no. 184,* 15 August 1943, 13 pp. [P]

495. Livingston, P. C. Report on effects of anoxia, carbon monoxide, and diabetes on the field of vision. Gt. Brit. FPRC. *F. P. R. C. 451,* undated, 2 pp. [P]

496. Maynard, F. L. Low pressure chamber demonstration of the effect of anoxia on night vision held at N. A. S. Grosse Ile, Michigan, 28 November 1945. U. S. Navy, Quonset Point. *Project X–580 (Av–299–f), Rept. no. 3,* 12 December 1945, 8 pp.

497. Motokawa, K. and K. Iwama. The electric excitability of the human eye as a sensitive indicator of oxygen deficiency. *Tôhoku J. exp. Med.,* 1949, *50–51:* 319–328.

498. Murray, G. D. The effect of acute anoxia upon flicker, dotting and handwriting tests in twenty untrained subjects. U. S. Navy, NATC, Pensacola, Fla., School of aviation medicine. *Project X–111 (Av–R7–5),* 15 February 1943, 4 pp. [P]

499. Peckham, R. H. Loss of visual contrast discrimination. U. S. Navy. NATC, Pensacola, Fla., School of aviation medicine. *Project X–153 (Av–R5–1),* 4 June 1943, 6 pp. [P]

500. Posternak, J. L'adaptation visuelle à l'obscurité au Jungfraujoch. *Helvet. physiol. pharm. Acta,* 1948, *6:* 516–523. (English summary.)

501. Posternak, J. Le champ visuel à l'altitude. *Helvet. physiol. pharm. Acta,* 1948, *6:* 524–527. [P]

502. Scobee, R. G. The effect of exhaustion and of moderate anoxia on ocular muscle balance. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 292, Rept. no. 1,* 18 July 1944, 3 pp. [P]

503. Seitz, C. P. and G. M. Smith. Auditory sensitivity under conditions of anoxia: A study of speech intelligibility. City College of New York, Psychological laboratory. 29 January 1942, 10 pp. [P]

504. Tschirren, B. and K. Wiesinger. Untersuchungen über den zeitlichen Verlauf des konsensuellen Pupillenreflexes beim Übergang in die Höhe. *Helvet. physiol. pharm. Acta,* 1948, *6:* 554–559. [P]

505. Zwahlen, P. and E. Grandjean. Variation des sensibilités cornéene et cutanée à l'altitude. *Helvet. physiol. pharm. Acta,* 1948; *6:* 471–473. (English summary.)

3. NERVOUS SYSTEM

Reports by the following authors are devoted to investigations of the effects of decompression hypoxia on psychological functioning and psychomotor performance: Anthony, Clarke, Liberman, Miles, Nims, Tepperman, and Wesley (*507*) 1943; Fabre, Rougier, and Broussin (*509*) 1948; Gantt, Thorn, and Dorrance (*512*) 1949; Gerathewohl (*514*) 1951; Grandjean (*515*) 1948; Green (*516*) 1947; Hall (*518*) 1950; Halstead (*519*) 1943; Klingman (*523 and 524*) 1947; Liberman, Miles, Nims, and Wesley (*527*) 1944; Mackenzie, Riesen, Bailey, Tahmisian, and Crocker (*532*) 1945; Ricketts, Adams, Alving, Bay, Bryan, Carmichael, Case, Halstead, and Landowne (*534*) 1945; Russell (*535*) 1948; Scow, Krasno, and Ivy (*536*) 1950; Smith (*538*) 1948; and Van Liere (*541*) 1942. These studies generally point out that of all tissues of the body, the nervous system is perhaps least capable of withstanding oxygen want.

According to Gellhorn and Ballin (*513*) 1950, normal and adrenal-demedullated rats anesthetized with pentothal show a greater susceptibility to electroshock-induced convulsions under moderate

degrees of hypoxia (280 mm. Hg for 10 minutes) than at normal barometric pressure. It was found that unanesthetized rats, shocked at a stage of hypoxia when righting reflexes are lost, responded more frequently with convulsions and showed more severe convulsions than under control conditions. On the contrary, it was observed that severe hypoxia leading to functional elimination of the cortex and brain stem reduced the susceptibility to convulsions. It was suggested by the authors that the increased susceptibility to convulsions in moderate anoxia was related to release of the subcortical structures.

Hypoxia tends generally to reduce spinal reflex action. For papers on this subject, reports by the following authors may be consulted: Guibert (*517*) 1951, Petrov (*533*) 1949, and Sillani (*537*) 1947. Beyne, Chauchard, and Chauchard, (*508*) 1947 determined variations in chronaxie in man in a chamber subjected to a simulated altitude of 4,500 to 5,000 meters. Chronaxie was determined on the median and radial nerves by inserted electrodes. It was found that under the conditions of these experiments chronaxie was doubled and sometimes quintupled. For a study of anoxic depolarization of frog nerves, a paper by Lorente de No (*530*) 1947 should be consulted.

For a detailed review of the histopathological changes within the central nervous system after exposure to high altitudes, hypoglycemia and other conditions associated with central hypoxia, a report by Hoff, Grenell, and Fulton (*520*) 1945 should be consulted. This report contains a very full bibliography. Under conditions of reduced barometric pressures, ganglian-cell changes correspond closely to those encountered in animals exposed to low oxygen mixtures at sea level. The cerebral cortex is usually spared. The medulla and cerebellar cortex are particular sites of election but damaged nerve cells are found scattered throughout the brain stem. In general, there are few or no changes in the spinal cord. In the affected ganglian cells the Nissl substance is characteristically fragmented or broken up into fine dustlike particles. The cytoplasm may be vacuolated or homogeneously stained. There may be swelling or shrinkage of the cells. The nuclei may be displaced, irregular in shape, shrunken or darkly staining, and amorphous. Varicosities of the dendrites are sometimes characteristic. Animals subjected to a single lethal exposure at a simulated altitude of 12,000 meters for 40 to 110 minutes do not tend to show neuropathological changes, nor are the lesions present in the brains of animals sacrificed after repeated short, daily, sublethal decompressions to this altitude. Exposure to single periods of decompression to 250 mm. Hg. for 33 to 104 hours does not result in histologically demonstrable lesions if the animals are sacrificed immediately after the experiment, although such animals usually die spontaneously some days later with marked changes in the brain. In general, pathological changes are most pronounced and widespread in animals succumbing to repeated decompression or dying some days after single exposures to low pressure.

Titrud and Haymaker (*540*) 1947 have presented a clinicopathological study of two cases of high altitude death with unusually long survival. They have also given a clinical report of a nonfatal case. In the two fatal cases, death occurred in 40 hours and 3 weeks after exposure to altitude. The third case, the nonfatal one, was observed for 3 weeks. The degree and duration of hypoxia in each case is not accurately known. In the first case, the accident occurred at higher than 20,000 feet. The patient was found unconscious 5 minutes after the completion of a bombing run. The second patient was exposed to an altitude of 24,000 feet for approximately 10 minutes. In the third case, exposure was at an altitude of 27,000 feet. In the first fatal case there was conspicuous necrosis of ganglian cells in the cerebral cortex, basal ganglia, cerebellum, and the anterior horns of the spinal gray matter. There was also degeneration of myelin in the internal capsule. In the second fatal case, the changes were virtually the same, except that the cerebral white matter, the brain stem, and spinal cord tended to be spared. In a report of observations at autopsy in 75 cases of high-altitude hypoxia, Lewis and Haymaker (*525*) 1949 found conspicuous evidence of circulatory failure. In most cases the blood in the heart and large vessels had not clotted. There were hemorrhages in the lungs, myocardium, submucosa of the intestinal tract, adventitia of the aorta, mastoid and petrosal sinuses, paranasal sinuses, and the middle and internal ear. Hemorrhages in the brain were small and sparse. Intracellular vacuoles, containing inclusions, were found throughout the body, but were especially prominent in the liver and the heart. Though the periods of hypoxia in question were rarely longer than 20 minutes, shrinkage and chromatolysis of ganglion cells were prominent. The cells of the cerebral cortex were mostly affected, especially in the hippocampus.

In an experimental series reported by Jensen, Becker, and Windle (*522*) 1949, young adult male guinea pigs were subjected to atmospheric conditions simulating an altitude of 30,000 feet in a decompression chamber for 6 hours daily, 6 days weekly up to 100, 150, 200, and 250 hours. At

appropriate times the experimental animals and controls were killed by perfusion of a solution of formaldehyde. The animals responded to reduced barometric pressure by remaining quiet, usually with episodes of physical distress, collapse, and apparent unconsciousness. After removal from the chamber, comparison with controls rarely revealed significant behavior changes or physical differences. No permanent neurological defects were observed. Exposure for 150, 200, and 250 hours resulted in retentive loss in ability to solve an alternation maze problem. All control animals solved the problem to the point of perfection. Focal areas of degeneration were discovered in the vermis of the cerebellum of all animals killed after 250 hours of exposure and in 3 of the 7 animals after 100 and 150 hours. Elsewhere in the brain there were small areas of shrinkage of impaired staining. For the most part, the tissues of the brain appeared normal and most regions looked exactly like the controls. The histological studies failed to reveal an anatomical basis for the defect in memory. However, the most striking memory defects occurred in the group of animals exposed to decompression for the maximum time, and it was in this group also that structural changes in the brain were most consistently revealed.

Lindenberg (*528*) 1951 pointed out that the duration of hypoxia preceding death affects the post-mortem morphological appearance of ganglion cells. In instantaneous death, the ganglion cells exhibited homogenization with and without shrinkage, vacuolation, and incrustation of the Golgi apparatus. When the brain was kept at body temperature, simple swelling appeared in 30 minutes, followed by homogenization and vacuolation in 6 hours. If death was preceded by severe hypoxia lasting 10 to 15 minutes, vacuolation seldom occurred and homogenization was incomplete; 30 minutes of hypoxia produced immediate post-mortem pyknosis and shrinkage; after hypoxia of 60 minutes the cells showed no noticeable changes between death and fixation. In a further report, Lindenberg (*520*) 1951 reported that in all cases of acute death, with fixation of the brain 8 to 46 hours after death, clasmatodendrosis of the astrocytes occurred. If severe hypoxia of less than 30 minutes' duration preceded death, clasmatodendrosis was accompanied by acute swelling, which did not occur if the hypoxic phase lasted 30 to 60 minutes. In cases of subacute death preceded by hypoxia lasting longer than 60 minutes, the astrocytes revealed size variations and curling of the dendrites. Clasmatodendrosis was absent even 48 hours after death. Cell changes after acute death were principally those following fresh, local disturbance of the circulation by an embolism.

For further studies on the effects of decompression hypoxia on the nervous system, papers by the following authors should be consulted: Adams, Alving, Bay, Bryan, Carmichael, Case, Halstead, Landowne, and Ricketts (*506*) 1943; Fleisch and Grandjean (*511*) 1948; Hoffman, Clark, and Brown (*521*) 1945; Lifshits (*526*) 1949; di Macco (*531*) 1946; Suzuki and Masuda (*539*) 1951; Volochov and Obraszova (*542*) 1950; and Fenn, Galambos, and Rahn (*510*) 1950.

506. Adams, W. R., A. S. Alving, E. B. Bay, A. H. Bryan, H. T. Carmichael, T. J. Case, W. C. Halstead, M. Landowne, and H. T. Ricketts. The effects of chronic intermittent anoxia in man; introduction, summary of results at 10,000 and 11,500 feet and conclusions. U. S. NRC–CAM. *C. A. M. rept. no. 160,* 20 July 1943, 7 pp.

507. Anthony, R. A., R. W. Clarke, A. Liberman, W. R. Miles, L. F. Nims, J. Tepperman, and S. M. Wesley. A comparison of the psychological effects of first and second hours of exposure to anoxia at 15,000 feet. U. S. NRC–CAM. Yale aeromedical research unit. *C. A. M. Rept. no. 141,* 8 June 1943, 7 pp.

508. Beyne, J., P. Chauchard, and B. Chauchard. Les facteurs conditionnant les variations d'excitabilité nerveuse en dépression atmosphérique chez l'homme. *C. R. Acad. Sci., Paris,* 1947, *225:* 437–439.

509. Fabre, R., G. Rougier, and J. Broussin. Quelques experiences rélatives à l'apparition d'une activité psycho-physiologique inconsciente au cours de l'anoxémie chez l'homme. *Méd. aeronaut.,* 1948, *3:* 29–44. [P]

510. Fenn, W. O., R. Galambos, A. B. Otis, and H. Rahn. Corneo-retinal potential in anoxia and acapnia. *J. appl. Physiol.,* 1950, *1:* 710–716. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1256.

511. Fleisch, A. and E. Grandjean. Der Tonus der Skelettmuskulatur im Höhenklima. *Helvet. physiol. pharm. Acta,* 1948, *6:* 474–483. (English summary.)

512. Gantt, W. H., G. W. Thorn, and C. Dorrance. Anoxia on conditional reflexes in dogs. *Fed. Proc. Amer. Soc. exp. Biol.,* 1949, *8:* 53.

513. Gellhorn, E. and H. M. Ballin. Further investigations on effect of anoxia on convulsions. *Amer. J. Physiol.,* 1950, *162:* 503–506. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 647. Abstr. [P]

514. Gerathewohl, S. J. Method for the analysis of psychomotor performance under hypoxia. *J. Aviat. Med.,* 1951, *22:* 196–206. [P]

515. Grandjean, E. Fonctions nerveuses à l'altitude. *Helvet, physiol. pharm. Acta,* 1948, *6:* 489–515. (English summary.)

516. Green, D. M. Variations in the effect of anoxia on performance. *Amer. J. Physiol.,* 1947, *151:* 588–592. [P]

517. Guibert R. *Effet d'un séjour à une altitude moyenne sur les seuils de la sensibilité cutanée et du réflexe rotulien.* Thèse (Méd.) Lausanne, 1951, 20 pp.

518. Hall, F. G. Factors affecting consciousness time at altitude. Part II. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *AF technical rept. no. 6009,* September 1950, 24 pp. [P]

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4. HEART AND CIRCULATION

For general studies of the effects of decompression hypoxia upon the heart and circulation, papers by the following should be consulted: Houston and Riley (*550*) 1947, Starr and McMichael (*561*) 1948, and Van Liere (*565*) 1942. The latter author has pointed out that under progressive hypoxia there is acceleration of the heart with alteration in systolic blood pressure, the pressure being maintained, rising and then gradually falling. The pulse pressure remains unchanged or increases. Within certain ranges there may be an increase in cardiac output which may play an important part in the capacity of the individual to withstand hypoxia and to acclimatize to high altitude. Coronary flow is said to increase greatly when oxygen is reduced to 8 or 9 percent. Moderate hypoxia may produce vagospasm and could in part account for the delay in the cardiac impulse. Severe anoxia probably produces delayed conduction by directly affecting conduction tissue. The electrocardiogram under conditions of hypoxia shows a diminished or inverted T-wave, lengthening of the P–R interval, and deformity of the QRS complex. Severe anoxia

may result in cardiac dilatation. Continued exposure to hypoxia may produce cardiac hypertrophy.

For studies on the effects of decompression hypoxia upon cardiac action with particular reference to the electrocardiogram, papers by the following should be consulted: Baum, Malmo, and Sievers (*544*) 1945; Kirschbaum (*551*) 1951; Plas, Tabusse, Missenard, and Goujon (*554*) 1947; Rotta (*555*) 1947; Schutz (*560*) 1948; and Wyss-Dunant (*569*) 1950.

For studies on the effects of decompression hypoxia upon blood pressure, papers by the following may be consulted: Franzblau, Vawter, Pestel, and Marbarger (*545*) 1951; Rotta and Miranda (*556*) 1949, Stavraky (*562*) 1945; Stavraky (*563*) 1946; Wezler and Frank (*566*) 1948; and Whitehorn (*567*) 1948. Papers on the effects of hypoxia on capillary circulation, fragility, and permeability have been reported by the following: Gabay (*546*) 1951; Henry, Klain, Movitt, and Meehan (*548*) 1946; Hopps and Lewis (*549*) 1947; Schmid (*558*) 1949; and Wiemers, Maurer, and Niklas (*568*) 1950. A paper on neurocirculatory collapse at altitude by Adler (*543*) 1950 and a study by Schneider (*550*) 1948 constituting a general review of the subject of circulation during hypoxia may be read.

Mitchell, Thompson, and Arnold (*553*) 1951 have studied the effects of intermittent exposure to high altitude on cardiovascular-renal lesions in hypersensitive rabbits. Sixty rabbits provided four treatment combinations: (1) controls; (2) hypersensitivity to horse serum; (3) acute exposure to high altitude; and (4) a combination of the hypersensitive state and altitude exposure. Qualitative and quantitative estimates of pathological lesions were made at the end of 28 days for the 4 groups of experimental animals. Under the conditions of this study, pathological evaluation of the animals showed that the protracted hypersensitive state when combined with the stress of altitude exposure resulted in a greater degree of heart and kidney damage than did either hypersensitivity or altitude stress alone.

For further studies of the effects of hypoxia upon the heart and circulation, papers by the following may be referred to: Kramer and Luft (*552*) 1950, Schaefer (*557*) 1948, and Vacca and de Franciscis (*564*) 1947.

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5. BLOOD

Papers by the following may be consulted for studies on the effects of decompression hypoxia on red cell formation and on polycythemia: Bonsdorff (*571*) 1948; Bühlmann, Wang, Wirz, and Verzár (*575*) 1951; Chiodi (*579*) 1951; Craven, Reissmann, and Chinn (*580*) 1951; Fave and Ringenbach (*582*) 1950; Hurtado, Merino, and Delgado (*585*) 1945; Merino (*588*) 1950; Merino and Reynafarje (*589*) 1949; Saathoff (*592, 593*), 1950–51; Uzhanskii (*595*) 1949; and Van Liere (*596*) 1942. Exposure to low barometric pressure environments causes a polycythemic response with wide variations. In general, however, the polycythemic response is directly proportional to the degree of hypoxia and its duration and continuity. There seems to be a limit beyond which the hypoxic stimulus will not induce a hematological response. When extremely severe, the hypoxia may produce a depression rather than a further stimulation of hematopoiesis. The polycythemia observed immediately on arrival at high altitude appears to be due to release of stored blood; for example, from the spleen. The polycythemia associated with repeated or constant exposure to low pressure environments is due to erythropoietic hyperactivity. Polycythemia of constant or intermittent hypoxia tends to show proportional elevation in circulating reticulocytes and in serum bilirubin. This latter suggests an increased rate of cellular destruction paralleling increased formation, but other factors such as insufficiency of the liver in pigment excretion due to hypoxic conditions may also play an etiological role in hyperbilirubinemia. The stimulating influence of hypoxia upon the hematopoietic system is restricted to formation of red blood corpuscles. Leukopoiesis is not affected. Moderate and temporary leukocytosis is sometimes observed on arrival at high altitudes, probably related to the release and mobilization of stored blood. Chronic hypoxia does not modify erythropoietic activity permanently; a person who has lived since birth at high altitudes and is brought to sea level shows, after some time, characteristics similar to those in persons who have always lived at sea level. Abnormal decrease in red blood corpuscles and hemoglobin may occur during early adaptation to sea-level pressure (Hurtado, Merino, and Delgado (*585*) 1945).

Regarding the effects of high-altitude hypoxia upon white blood count Grandjean, Arnold, Berney, Guibert, Jaquerod, and Magnin (*583, 584*) 1949 found that in 8 healthy subjects who remained at an altitude of 1,750 meters for 3 weeks, there was a significant rise, not only in the red blood count and hemoglobin level, but also in the white blood count. There was an absolute increase in the numbers of polymorphonuclear leukocytes, lymphocytes, and monocytes.

Some reports, for example, that of Delachaux and Tissieres (*581*) 1946, indicate a rise not only of hemoglobin but also of the myoglobin level during acclimatization to high altitude. However, Bowen and Poel (*573*) 1948 and Bowen and Eads (*572*) 1949 have found no increase but rather a diminution in the myoglobin level in animals subjected to simulated high altitudes. In the former study (*573*), rats were exposed for 2 to 52 weeks, for 4 hours daily to 282 mm. Hg (a simulated altitude of 25,000 feet). In these animals, the hematocrit and hemoglobin values increased to 25 and 66 percent, respectively, over the averages for the controls. The myoglobin, however, consistently showed no significant change from that of the controls. Also the results showed that 2 to 8 times more hemoglobin was retained by the muscles of the exposed animals than

by the controls and that the amount retained varied directly with the hematocrit value. In the report of Bowen and Eads, dogs were exposed to a simulated altitude of 18,000 feet, 16 hours a day, 6 days a week for 6 months. At the end of the exposure period, the dogs were killed by deep anesthesia and exsanguination. Samples of various muscles including the heart and diaphragm were removed for analysis. In all the exposed dogs, the hemoglobin content increased markedly during the exposure, but the average myoglobin content of the muscles studied was less in the exposed dogs than in the unexposed. In a report by Reismann, Hoelscher, Topka, Criscuolo, and Burkhardt (*591*) 1951, the hemoglobin metabolism during the development and disappearance of polycythemia induced by hypoxia was studied by measuring the total circulating hemoglobin and the daily bile pigment excretion in dogs with bile fistulas before, during, and after prolonged periods of exposure to a simulated altitude of 20,000 feet. The increased erythropoiesis during the first weeks of altitude exposure was accompanied by a significant increase in bile-pigment output. No differences were seen in the life span of the red cells at ground level and during altitude exposure. The return of the number of red cells to normal after reaching ground level was achieved by the combined effect of a depression of erythropoiesis and an increase in blood destruction. The latter accounted for 21 to 39 percent of the hemoglobin which disappeared from the circulation after return to sea level.

The effect of acute hypoxia upon the blood histamine level has been studied by Burkhardt, Flickinger, and Adler (*576*) 1949. These authors have reported that the blood histamine content of dogs as measured by biological assay may increase tenfold or more in response to continuous hypoxia at a simulated altitude of 18,000 feet. The increase in histamine reached a peak on the fourth day of exposure and may be correlated with the clinical status of the dogs which at that time were apathetic, lethargic, and had lost appetite. After the peak had been reached on the fourth day, the histamine level began to decline until it again attained the control level about 7 or 8 days later; that is to say, after a total of about 12 days of continuous exposure. The decrease in histamine level seemed to be correlated with clinical symptoms in that gradually over the period of histamine decline, the animals lost their apathy and began to eat normally. When the dogs were returned to the ground level for 8 days, a reexposure to 18,000 feet failed to elicit the same marked degree of histamine response noted on the first exposure. A later study by Burkhardt, Flickinger, Coulson, Criscuolo, and Adler (*577*) 1951 revealed no increase in blood histamine in dogs, cats, and human beings subjected to acute hypoxia for periods of 1½ hours.

Plasma, cell and blood volumes, and total circulating hemoglobin were determined in a group of dogs before, during, and after acclimatization to 20,000 feet simulated altitude by Reissmann (*590*) 1951. During altitude exposure the plasma volume decreased gradually to a constant level, which was 75 percent of the ground-level value. The cell volume reached a plateau of 170 percent of the ground-level value in the fifth week of exposure and returned to normal within 6 weeks after exposure had been discontinued. The total circulating hemoglobin paralleled the cell volume, and in some animals increases of 200 grams of hemoglobin were observed during 5 weeks of exposure. The total blood volume remained almost constant during the first 2 weeks of exposure, then increased slowly and reached a plateau at 125 percent of the ground-level value in the fifth week of exposure.

Mobilization of red cells from the spleen in severe hypoxia has been reported by Kramer and Luft (*586*) 1951. These observations recorded contraction of the spleen in nembutalized dogs during acute hypoxia. This response did not appear early, but was a terminal event immediately preceding respiratory failure. Loss in spleen weight during contraction coincided with an increase in systemic hemoglobin content. During the refilling phase of the spleen in recovery from hypoxia, the same inverse relationship was evident as the systemic hemoglobin returned to the control level. An estimate of the hemoglobin concentration in stored blood based upon the amount of blood released by the spleen led the authors to the conclusion that the splenic stores consist almost entirely of packed red cells. Continuous records of the hemoglobin content in the splenic vein showed very rapid changes in the final stages of hypoxia, with peak values twice as high as in arterial blood. During recovery, the hemoglobin level in the splenic vein was slightly lower than in the artery, signifying the retention of red cells at this time. During control periods, with the animal breathing air, spontaneous rhythmic fluctuations were frequently observed in the hemoglobin content of blood in the splenic vein. During hypoxia, the oxygen saturation of venous blood from the spleen remained consistently higher than in arterial blood and even increased when splenic contraction reached its peak. It was concluded by the authors that in the critical phase of hypoxia, the spleen of the dogs releases large amounts of red

cells with a relatively high oxygen content into the portal venous system.

For further studies on the effects of decompression hypoxia on the blood, papers by the following authors should be consulted: Beutler and Stämpfli (*570*) 1948; Buhlmann and Hofstetter (*574*) 1951; Charnyi, Strltsov, Syrkina, and Kraspovitskaia (*578*) 1946; Malmejac, Cruck, and Neverre (*587*) 1950; and Scano and Gnudi (*594*) 1950.

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596. **Van Liere, E. J.** Effect of anoxia on the blood, pp. 33–58 in: *Anoxia. Its effect on the body.* Chicago, The University of Chicago Press, 1942, 269 pp. [R]

6. RESPIRATION

For studies of respiratory metabolism of human subjects during exposure to decompression hypoxia, papers by the following authors should be consulted: D'Angelo (*597, 598*) 1946, Houston and Nez (*602*) 1946, Riley and Houston (*606*) 1948, Rothschuch (*608*) 1947, and Schaefer and Alvis (*610*) 1951. The following authors have contributed reports dealing with alveolar and arterial gas tensions in hypoxia: Miller, Taylor, and Heagan (*604*) 1946; Lilienthal and Riley (*603*) 1946; Gemmill and and Malone (*599*) 1945; Grutering, Opitz, and Palme (*600*) 1944; Hoffman, Clark, and Brown

(*601*) 1945; Scano (*609*) 1951; and Winterstein (*612*) 1950. For general articles on the effects of hypoxia on respiration, papers by Nims (*605*) 1946 and Van Liere (*611*) 1942 should be consulted. For other studies on respiration, the reader is referred to papers by Rodbard (*607*) 1946 and Winterstein (*613*) 1950.

597. D'Angelo, S. A. The respiratory metabolism of human subjects during prolonged exposures to simulated altitudes of 8,000 and 10,000 feet. *Amer. J. Physiol.*, 1946, *146:* 710–722.

598. D'Angelo, S. A. The respiratory exchange in human subjects during prolonged exposures to moderately low simulated altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 20.

599. Gemmill, C. L. and M. E. Malone. The physiological effects of anoxia and exercise. The relationship between alveolar air oxygen tensions and arterial blood oxygen saturations. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project X–484 (AV–258–f), Rept. no. 1,* 15 May 1945, 20 pp. [P]

600. Grütering, F., E. Opitz, and F. Palme. Darstellung der Höhenanpassung im Gebirge durch Sauerstoffmangel. IV. Steigerung der alveolaren Höhenfestigkeit untersucht am Schriftbild. *Pflüg. Arch. ges. Physiol.*, 1944, *248:* 376–386. [P]

601. Hoffman, C. E., R. T. Clark, Jr., and E. B. Brown, Jr. Blood oxygen saturations and duration of consciousness in anoxia at high altitudes. *Amer. J. Physiol.*, 1945, *145:* 685–692.

602. Houston, C. S. and M. Nez. Relation of pulmonary ventilation to arterial oxygen. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine. *Project X–675,* 20 January 1946, 11 pp.

603. Lilienthal, J. L. and R. L. Riley. An experimental analysis in man of the oxygen pressure gradient from alveolar air to arterial blood during rest and exercise at sea level and at altitude. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine. *Project X–484 (Av–258–f), Rept. no. 3,* 23 February 1946, 33 pp.

604. Miller, R. A., C. B. Taylor, and B. Heagan. The oxygen content of arterial blood of dogs exposed to diminished pressures in a decompression chamber. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 414, Rept. no. 1,* 14 August 1946, 7 pp.

605. Nims, L. F. Respiration. *Annu. Rev. Physiol.*, 1946, *8:* 99–116. [R]

606. Riley, R. L. and C. S. Houston. Composition of alveolar air and rate of pulmonary ventilation during long exposure to high altitude. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine and research. *Project NM 001 013 (X–720) (Av–376–s), Rept. no. 7,* 8 September 1948, 5 pp. [P]

607. Rodbard, S. The effect of oxygen, altitude, and exertion on breath-holding time. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 88.

608. Rothschuh, K. E. Zur Frage eines "Sparstoffwechsels" bei kurzdauerndem Sauerstoffmangel. *Pflüg. Arch. ges. Physiol.*, 1947, *249:* 175–190. [P]

609. Scano, A. Ricerche sulla resistenza alla depressione barometrica. Nota I. Tensione dei gas alveolari, consumo di O_2 e limiti de ricupero nel coniglio sottoposto a depressione barometrica. *Riv. Med. aeronaut.*, 1950, *13:* 507–550. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1213.

610. Schaefer, K. E. and H. J. Alvis. The effect of inhalation of low oxygen concentration (10.5% O_2 in N_2) over a period of 33 minutes on respiration, pulse rate, arterial oxygen saturation (oximeter) and oxygen uptake. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 015.03.02, Rept. no. 175,* 8 August 1951, 32 pp. [P]

611. Van Liere, E. J. Effect of anoxia on respiration. pp. 101–127 in: *Anoxia, Its effect on the body.* Chicago, The University of Chicago Press. 1942, 269 pp. [R]

612. Winterstein, H. Die alveolare Kohlensäurespannung in mittleren Hôhen. (1800 m.) *Arch. int. Pharmacodyn.*, 1950, *82:* 67–79. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1210.

613. Winterstein, H. Effets mécaniques de l'air raréfié. *Concours méd.*, 1950, *72:* 233–234. [P]

7. ALIMENTARY TRACT

For an extensive monograph on the influence of law barometric pressure on the process of digestion, reference is made to a report by Razenkov (*616*) 1948. This work includes material on the influence of decreased barometric pressure on salivary secretion and secretory activity of the gastric glands. An article by Van Liere (*617*) 1942 may also be consulted. This author pointed out that under conditions of hypoxia, hunger contractions in the dog were decreased in amplitude and that gastric motility was reduced. There is a delay in gastric emptying time in both dogs and man. Anemic anoxia is stated to stimulate hunger contraction and delay gastric emptying. Histotoxic anoxia produced by barbiturates, bromides, and other drugs all caused prolonged gastric emptying. Compared with the central nervous system, the gastrointestinal tract is stated to be relatively resistant to hypoxia. Ranges of hypoxia compatible with life would not interfere with proper nourishment of the body so far as absorption from the gut is concerned. Van Liere, Stickney, and Northup (*618*) 1950 and (*619*) 1951 reported that the propulsive motility of the small intestine in rats was decreased by hypoxia. It was reasoned that if rats were acclimatized to low oxygen tensions, exposure to altitude would no longer produce this effect. A group of albino rats were accordingly acclimatized by subjecting them to a simulated altitude of 24,000 feet by approximately 3 hours each day for 26 or 62 days. These acclimatized rats were paired with normal rats which were as nearly alike in weight and age as possible. A pair of these rats was given 2 cu. cm. of a charcoal-acacia mixture by stomach tube. After allowing 10 minutes for some of this material to enter the small intestine, both rats were placed in a low-pressure chamber at a pressure of 254 mm. Hg (simulated altitude, 28,000 feet). At the end of 30 minutes they were removed from the chamber and decapitated. The small intes-

tine was removed, slit open, and the distance the charcoal had traversed measured. It was observed that the propulsive motility was significantly less in the unacclimatized than in the acclimatized animals. This was interpreted by the authors to mean that the effect of hypoxia upon the propulsive motility of the small intestine could be used as a criterion for acclimatization.

MacLachlan (*615*) 1946 found that rats exhibited an initial acceleration of stomach emptying on exposure to diminished oxygen tension. He concluded that decreased rate of absorption of fat in rats subjected to hypoxia cannot be explained on the basis of prolonged gastric emptying time. In studies on the effects of hypoxia on gastric secretory functions, Karvinen and Karvonen (*614*) 1949 subjected human subjects (3 normal and 1 achlorohydric subject) to a simulated altitude of 5,000 meters. Alcohol and carbaminolcholine were used as stimuli. In the carbaminolcholine tests the volume of gastric juice collected at 5,000 meters was, on the average, one-fifth of the corresponding value at sea level. The acid secreted was one-ninth and the amount of pepsin was one-twelfth of sea-level values. The total chloride value followed a course comparable to the values for titratable acidity, both at sea level and at 5,000 meters. In the alcohol tests, the secretion of the different components was fairly uniformly decreased at altitude. However, suppression of secretion was less pronounced than in the carbaminolcholine tests. The secretions of the achlorohydric stomach seemed unaffected by the degree of hypoxia imposed.

614. Karvinen, E. and M. J. Karvonen. On the anoxic suppression of the gastric secretory functions. *Ann. Med. exp. Fenn.*, 1949, *27:* 59–72. [P]

615. MacLachlan, P. L. Effect of anoxic anoxia on gastric emptying time of rats fed corn oil. *Proc. Soc. exp. Biol., N. Y.*, 1946, *63:* 147–148.

616. Razenkov, I. P. *Vliianie ponizhennogo barometricheskogo davleniia.* [Influence of low barometric pressure on process of digestion.] Izdatelstvo Akademii Medizinskih Nayk S. S. S. R. Moskva, 1948, 167 pp. (Russian text.)

617. Van Liere, E. J. Effect of anoxia on the alimentary tract. pp. 159–185 in: *Anoxia. Its effect on the body.* Chicago, The University of Chicago Press, 1942, 269 pp. [R]

618. Van Liere, E. J., J. C. Stickney, and D. W. Northup. Effect of acclimatization on motility of small intestine during anoxia. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 128.

619. Van Liere, E. J., J. C. Stickney, and D. W. Northup. The effect of acclimatization on the propulsive motility of the small intestine during anoxia. *Proc. Soc. exp. Biol. Med.*, 1951, *76:* 102–103. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1238. [P]

8. METABOLISM

For studies of weight loss and retardation of growth produced by decompression anoxia, papers by Stickney (*648* and *649*) 1946 and Altland (*620*) 1948 should be consulted. A very complete article by Altmann (*621*) 1949 provides an excellent review of liver changes produced experimentally in cats by hypoxia. This article contains 463 references to the literature. References to articles by the following authors are recommended to readers desiring recent studies on the effects of hypoxia on carbohydrate metabolism: Boutwell, Cilley, Krasno, Ivy, and Farmer (*625*) 1951; Gellhorn and Safford (*632*) 1948; Keyes and Kelley (*633* and *634*) 1949; Langley, Nims, and Clarke (*637*) 1950; Langley, Nims, Harvey, and Clarke (*638*) 1943; McDonald (*639*) 1947; Nims, Langley, and Clarke (*643*) 1946; Saviano and Vacca (*646*) 1950; Stickney, Northup, and Van Liere (*650, 651*) 1948; Van Liere, Stickney, and Northup (*654, 655*) 1948; Van Middlesworth (*656*) 1946; and Wickson and Morgan (*661*) 1946. In general, acute decompression hypoxia results in decreased glucose tolerance manifested by prolonged elevation of the blood sugar levels and by failure to return to normal fasting volumes as early as at ground level. Insulin tolerance tests reveal a decreased insulin response in animals exposed to simulated altitudes.

Murray and Morgan (*641*) 1946 found that ascorbic acid-deficient guinea pigs had a significantly higher blood sugar level and probably significantly lower liver and carcass glycogen levels than pair-fed normal animals 6 hours after they were fed glucose following a 24-hour fast. The intestinal absorption of the sugar was less complete in the deficient animals. When similarly paired but fasting animals were exposed to hypoxia (349 mm. Hg for 24 hours), the deficient group was able to maintain or increase blood sugar and glycogen stores more effectively than did the normal. Fasting, deficient guinea pigs at ordinary atmospheric pressure had lower carbohydrate stores than did those under hypoxia, but this was not true for the normal animals. The ascorbic acid-deficient guinea pigs were found to have a significantly increased size of the adrenal glands, as compared with their paired controls. The lipid content of the livers and carcasses of the deficient animals was found to be nearly the same as in the normal, whether the animals had been subjected to hypoxia or not. The sudden loss of weight in the former was therefore considered to be due probably to dehydration. The liver-lipid values were increased in both groups after exposure to hypoxia. Oxygen consumption was not altered

by the ascorbic acid deficiency and no changes were seen in the thyroid glands. The reduced glycogen and increased blood sugar exhibited by the ascorbic acid-deficient guinea pigs following glucose feeding were considered by the authors to be in accord with the theory that the adrenal medullary mechanism is hyperactive in this deficiency. The increased size of the adrenal glands, rapid dehydration, and gluconeogenesis of the deficient animals under hypoxia point, according to the authors, to similar compensatory hyperactivity of the adrenocortical mechanism.

According to Krasno, Cilley, Boutwell, Ivy, and Farmer (*635*) 1950, repeated exposure of human subjects to a simulated altitude of 18,000 feet without additional oxygen resulted in a decrease in the daily urinary excretion of ascorbic acid from an average of 33.6 mg. down to 12 mg. The plasma level of ascorbic acid decreased from an average control level of 0.73 mg. percent down to 0.58 mg. percent during the last week of exposure. The authors suggested liberal quantities of fruit or fruit juice in the diets of persons subjected to continuous or discontinuous hypoxia or hyperventilation. Repeated exposure to a simulated altitude of 18,000 feet without supplemental oxygen did not affect the urinary output of thiamine, riboflavin, alpha-ketoglutaric acid, pyruvic acid, or acetone bodies. According to Mitchell and Edman (*640*) 1951, conditions of hypoxia may increase the requirements for ascorbic acid, thiamine, and nicotinic acid. Vitamin supplements to adequate diets have not been proved to be effective in increasing tolerance to hypoxia in man; particularly vitamin A supplement does not increase light sensitivity.

For studies on the effects of hypoxia upon respiratory catalysts, papers by the following may be consulted: Beinert, Maier-Leibnitz, Richey, and Reissman (*622*) 1950; Lalli and Tagliamonte (*636*) 1951; Seabra (*647*) 1947; Vannotti (*659*) 1946; and Voegtli (*660*) 1948. Tissue response to pathological oxygen deficiency is characterized by a significant increase of the levels of cytochrome C and of iron as well as biologically active complexes and of vitamins of the B group which are as coenzymes in the formation of the ferments indispensable to cellular metabolism.

Exposure to decompression hypoxia tends to increase the excretion of 17-ketosteroids in the urine. For such studies, papers by the following may be consulted: Biget (*623*) 1950, Burrill and Ivy (*628*) 1950, Cook (*629*) 1945, and Davidson (*631*) 1950. Van Middlesworth (*657*) 1950 and Van Middlesworth and Berry (*658*) 1951 have reported that hypoxia results in a decreased rate of uptake of radioactive iodine by the thyroid gland. In these experiments, rats fed a stock diet with a low iodide content were rapidly adapted to severe hypoxia by exposure to an equivalent altitude of 27,000 feet (258 mm. Hg) at 11 to 14° C. for 2 to 4 hours. After this exposure, the low iodide rats were injected intraperitoneally with 10 microcuries of carrier-free I^{131}. The barometric pressure was then reduced to 177 mm. Hg (35,000 feet equivalent altitude) for 8 to 12 hours. The thyroid glands of the hypoxic series contained one-fourth as much radioactivity as controls.

For studies on acid-base balance as affected by exposure to decompression hypoxia, papers by the following may be consulted: Boutwell, Farmer, and Ivy (*626*) 1950; Nims, Bunting, Ordway, and Clarke (*642*) 1943; Ochwadt (*644*) 1947; and Riley, Houston, and Jarvis (*645*) 1946. Additional references on the effects of decompression hypoxia upon metabolism are given as follows: Blood, Elliott, and d'Amour (*624*) 1946; Brobeck, Clarke, DuBois, Grenell, Liberman, Murphy, Nims, Patton, and Tepperman (*627*) 1943; Cook and Strajman (*630*) 1946; Tepperman, Tepperman, and Patton (*652*) 1944; and Van Liere (*653*) 1942.

620. Altland, P. D. Recovery rate from some of the effect of chronic intermittent hypoxia in rats. *Anat. Rec.*, 1948, *101:* 668. Abstr. [P]

621. Altmann, H. W. Über Leberveränderungen bei allgemeinem Sauerstoffmangel nach Unterdruckexperimenten an Katzen. *Frankfurt. Z. Path.*, 1949, *60:* 376–494. [R] [P]

622. Beinert, H., H. Maier-Leibnitz, E. O. Richey, and K. R. Reissmann. Further investigations on the injections of respiratory catalysts in an attempt to improve hypoxia tolerance. Studies on the incorporation of injected cytochrome C into tissue cells. USAF. Randolph Field, Tex. School of aviation medicine. Department of pharmacology and biochemistry. *Project 21–02–054, Rept. no. 1,* May 1950, 11 pp. [P]

623. Biget, P. Action de la dépression atmosphérique sur l'élimination urinaire des céto–17–steroïdes chez l'homme. *C. R. Soc. Biol., Paris,* 1950, *144:* 1091–1092. [P]

624. Blood, F. R., R. V. Elliott, and F. E. d'Amour. The physiology of the rat in extreme anoxia. *Amer. J. Physiol.*, 1946, *146:* 319–329. [P]

625. Boutwell, J. H., J. H. Cilley, L. R. Krasno, A. C. Ivy, and C. J. Farmer. Effect of repeated exposure of human subjects to hypoxia on glucose tolerance, excretion of ascorbic acid, and phenylalanine tolerance. *J. appl. Physiol.*, 1950, *2:* 388–392. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 540. Abstr.

626. Boutwell, J. H., C. J. Farmer, and A. C. Ivy. Studies on acid-base balance before and during repeated exposure to altitude, or to hypoxia and hyperventilation. *J. appl. Physiol.*, 1950, *2:* 381–387.

627. Brobeck, J. R., R. W. Clarke, D. DuBois, R. G. Grenell, A. M. Liberman, H. T. Murphy, L. F. Nims, D. W. Patton, and J. Tepperman. A biochemical study of

the effect of anoxia on exercise performance in human subjects. U. S. NRC–CAM. Yale Aeromedical Research Unit. *C. A. M. rept. no. 250,* 1 December 1943, 18 pp.

628. **Burrill, M. W. and A. C. Ivy.** Excretion of neutral 17-ketosteroids in human subjects repeatedly exposed to hypoxia under conditions of simulated high altitude. *J. appl. Physiol.,* 1950, *2:* 437–445. *Abstr. World Med.,* 1950, *8:* 232.

629. **Cook, S. F.** The inhibition of animal metabolism under decompression. *J. Aviat. Med.,* 1945, *16:* 268–271. [P]

630. **Cooks, S. F. and E. Strajman.** The effect of decompression on human metabolism during and after exercise. *J. industr. Hyg.,* 1946, *28:* abstract section: 47. U. S. NRC–CAM. Division of medical sciences. *OEMcmr–196, C. A. M. rept. no. 406,* 9 January 1945, 10 pp.

631. **Davidson, I. L.** The excretion of urinary total neutral 17-ketosteroids during anoxia. Gt. Brit. FPRC. RAF Institute of aviation medicine. *F. P. R. C. 739,* July 1950, 2 pp. [P]

632. **Gellhorn, E. and H. Safford.** Influence of repeated anoxia, electroshock and insulin hypoglycemia on reactivity of sympathetico-adrenal system. *Proc. Soc. exp. Biol., N. Y.,* 1948, *68:* 74–79. [P]

633. **Keyes, G. H. and V. C. Kelley.** Study of effects of altitude anoxia on glucose metabolism. 1. The glycogenic effect of adrenal cortical extract. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–02–030, Rept. no. 1,* February 1949, 6 pp. [P]

634. **Keyes, G. H. and V. C. Kelley.** A study of effects of altitude anoxia on glucose metabolism. The glucose tolerance of dogs as altered by atmospheric decompression. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–02–030, Rept. no. 2,* March 1949, 8 pp. [P]

635. **Krasno, L. R., J. H. Cilley, J. H. Boutwell, A C. Ivy, and C. J. Farmer.** Effect of repeated exposure of human subjects to 18,000 feet without supplemental oxygen, to hyperventilation, and to 35,000 feet with 100 percent oxygen for one hour, on ascorbic acid excretion and plasma level and on urine pH. *J. Aviat. Med.,* 1950, *21:* 283–292 and 312.

636. **Lalli, G. and B. Tagliamonte.** Comportamento del ferro totale et di quello tissulare nella milza e nel fegato, nei suoi rapporti con l'emoglo-binemia, in conigli sattoposti ad anossia discontinua ripetuta. *Riv. Med. aero., Roma,* 1951, *14:* 641–649. (English, French, German, and Spanish summaries.) [P]

637. **Langley, L. L., L. F. Nims, and R. W. Clarke.** Role of CO_2 in the stress reaction to hypoxia. *Amer. J. Physiol.,* 1950, *161:* 331–335. [P]

638. **Langley, L. L., L. F. Nims, T. S. Harvey, and R. W. Clarke.** Anoxia, carbon dioxide and liver glycogen. U. S. NRC–CAM. Yale aeromedical research unit. *C. A. M. rept. no. 108,* January 1943, 9 pp.

639. **McDonald, R.** Effects of altitude anoxia on glucose metabolism. USAF. Randolph Field, Tex. School of aviation medicine. *Project 502, Rept. no. 1,* 30 September 1947, 1 p. [P]

640. **Mitchell, H. H. and M. Edman.** Diet at altitude. pp. 96–151 in: *Nutrition and climatic stress.* Springfield, Charles C. Thomas. 1951, 234 pp. [R]

641. **Murray, H. C., and A. F. Morgan.** Carbohydrate metabolism in the ascorbic acid-deficient guinea pig under normal and anoxic conditions. *J. biol. Chem.,* 1946, *143:* 401–410.

642. **Nims, L. F., H. Bunting, N. K. Ordway, and R. W. Clarke.** Anoxic anoxia and acid-base balance. U. S. NRC–CAM. Yale aeromedical research unit. *C. A. M. rept. no. 107,* 18 January 1943, 5 pp.

643. **Nims, L. F., L. L. Langley, and R. W. Clarke.** Anoxia, carbon dioxide and liver glycogen. *Fed. Proc. Amer. Soc. esp. Biol.,* 1946, *5:* 76.

644. **Ochwadt, B.** Über Bicarbonatausscheidung und Kohlensäuresystem in Harn während akuter Hypoxie. *Pflüg. Arch. ges. Physiol.,* 1947, *249:* 452–469. [P]

645. **Riley, R. L., C. S. Houston, and W. H. Jarvis.** A study of the physiological changes which occur during acclimatization to high altitude. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project X–720, Rept. no. 4,* 21 September 1946, 14 pp.

646. **Saviano, M. and C. Vacca.** Richerche sui rapporti fra anossia e funzione insulare del pancreas. *Riv. Med. aero., Roma,* 1950, *13:* 171–188. (English, French, Spanish, and German summaries.)

647. **Seabra, P.** Oxidase and aviation. Influence of atmospheric decompression on the blood oxidase and resistance to infection. *J. Aviat. Med.,* 1947, *18:* 289–296. [P]

648. **Stickney, J. C.** The effect of various degrees of intermittent anoxia on body weight loss in normal rats. *Fed. Proc. Amer. Soc. exp. Biol.,* 1946, *5:* 101.

649. **Stickney, J. C.** Effect of anoxic anoxia on body weight loss in rats. *Proc. Soc. exp. Biol., N. Y.,* 1946, *63:* 210–212.

650. **Stickney, J. C., D. W. Northup, and E. J. Van Liere.** Blood sugar and dextrose tolerance during anoxia in the dog. *Amer. J. Physiol.,* 1948, *154:* 423–427.

651. **Stickney, J. C., D. W. Northup, and E. J. Van Liere.** Effect of anoxia on the glucose tolerance curve of dogs. *Fed. Proc. Amer. Soc. exp. Biol.,* 1948, *7:* 120.

652. **Tepperman, J., H. M. Tepperman, and B. W. Patton.** Effects of low barometric pressure on the chemical composition of the adrenal glands and blood of rats. U. S. NRC–CAM. Yale aeromedical research unit. *Rept. no. 26,* 13 June 1944, 8 pp. *Endocrinology,* 1947, *41:* 356–363.

653. **Van Liere, E. J.** Metabolism and anoxia. pp. 196–200 in: *Anoxia. Its effect on the body.* Chicago, The University of Chicago Press. 1942, 269 pp.

654. **Van Liere, E. J., J. C. Stickney, and D. W. Northup.** Blood sugar response to anoxia during acclimatization. *Amer. J. Physiol.,* 1948, *155:* 10–14. [P]

655. **Van Liere, E. J., J. C. Stickney, and D. W. Northup.** Effect of acclimatization on blood sugar response to anoxia. *Fed. Proc. Amer. Soc. exp. Biol.,* 1948, *7:* 126–127. [P]

656. **Van Middlesworth, L.** Glucose ingestion during severe anoxia. *Amer. J. Physiol.,* 1946, *146:* 491–495. [P]

657. **Van Middlesworth, L.** Metabolism of I^{131} during acute adaptation to anoxia. *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 128–129.

658. **Van Middlesworth, L. and M. M. Berry.** Iodide metabolism during anoxia, nephrectomy, trauma, avitaminoses and starvation in the rat. *Amer. J. Physiol.,* 1951, *167:* 576–580. [P]

659. **Vannotti, A.** The adaptation of the cell to effort, altitude and to pathological oxygen deficiency. *Schweiz. med. Wschr.,* 1946, *76:* 899–903. (French and German summaries.) [P]

660. **Voegtli, W.** Das Verhalten der Erythrocytenphosphatase bei 0_2 Mangel. *Helvet, physiol. pharm. Acta,* 1948, *6:* C69–C70. [P]

661. **Wickson, M. E. and A. F. Morgan.** The effect of riboflavin deficiency upon carbohydrate metabolism in anoxia. *J. biol. Chem.*, 1946, *162:* 209–220. [P]

9. KIDNEY

Exposure of human subjects to low partial pressures of oxygen equivalent to 15,000 feet altitude for 2 hours in experiments carried out by Anthony, Clarke, Liberman, Nims, Tepperman, and Wesley (*662*) 1943 tended to alkalinize the urine. The data presented, together with evidence in the literature, indicated to the authors that the principal changes in kidney function consist in an increase in bicarbonate elimination and a decreased phosphate elimination. Reduction of renal excretion of phosphorus in human subjects during prolonged exposures to simulated altitudes of 8,000 and 10,000 feet under conditions of restricted food and water intake was also reported by D'Angelo (*663*) 1946. No appreciable change in total urine output from ground-level values was found to occur in these experiments. According to D'Angelo (*664*) 1946, the most characteristic feature of urine elimination was the considerable degree of variation encountered from run to run despite the carefully controlled food and water intake. The reduction of total urinary excretion of inorganic phosphorus became apparent early in the exposure period at either the 8,000-foot or 10,000-foot level. The rate of excretion increased with increasing exposure time. The reduced phosphorus output bore no relationship to the total urine output, nor could it be directly correlated with changes in respiratory metabolism or in the sugar level. In experiments carried out on medical students by Kleinschmidt (*667*) 1948, exposure to 3,000 to 4,000 meters equivalent altitude resulted in a slight increase in urinary output. The increase was more definite at 5,000 meters and at 6,000 meters. With further increases in altitude, a pronounced decrease in urinary secretion occurred.

Observations on the effects of altitude hypoxia on renal function have been reported by Kelley and McDonald (*666*) 1948 and McDonald and Kelley (*669*) 1948. In the latter report, five dogs were subjected to renal function studies at ground level and at simulated altitudes of 18,000 feet and 24,000 feet. The glomerular filtration rate in these animals was either decreased, increased, or unaffected, depending upon the reaction of the individual animal to reduced ambient pressure. The effective renal plasma flow was increased in all dogs at an altitude of 18,000 feet, and was further increased in one dog, but decreased below ground level values in the remaining dogs at 24,000 feet. In the former report it was stated that in 2 or 3 animals a decrease in the maximal ability to absorb glucose (Tm$_G$) was observed at 18,000 feet as compared to the ground-level values, but in the third animal no change was evident. In none of the animals was there any appreciable difference between the value obtained at 18,000 feet and the value at 24,000 feet.

For a study of histopathological changes in the kidneys of mice subjected to hypoxia, a paper by Grattarola and Passerni (*665*) 1951 may be consulted. In animals subjected to a simulated altitude of 10,000 meters, there was intense cloudy swelling of the convoluted tubules with congestion in the glomeruli.

For further studies on the effects of hypoxia on renal functions, papers by Lalli (*668*) 1950 and Ochwadt (*670*) 1947 may be consulted.

662. **Anthony, R. A., R. W. Clarke, A. Liberman, L. F. Nims, J. Tepperman, and S. M. Wesley.** Renal function in man at reduced partial pressures of oxygen. U. S. NRC–CAM. Yale aeronautical research unit. *C. A. M. rept. no. 138,* 25 May 1943, 1 p.

663. **D'Angelo, S. A.** Urinary output and phosphorus excretion in human subjects during prolonged exposures at low simulated altitudes. *Proc. Soc. exp. Biol., N. Y.*, 1946, *62:* 13–17. [P]

664. **D'Angelo, S. A.** Urine volume and phosphorus excretion in human subjects during prolonged exposures to moderately low simulated altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 21.

665. **Grattarola, G. V. and P. G. Passerni.** Contributo sperimentale allo studio dell istopatologia del rene in ipossia. *Riv. Med. aero., Roma,* 1951, *14:* 668–672. (English, French, German, and Spanish summaries.) [P]

666. **Kelley, V. C. and R K. McDonald.** Further observations on the effects of altitude anoxia on renal function. *Amer. J. Physiol.*, 1948, *154:* 201–206.

667. **Kleinschmidt, K.** Über die Harnsekretion in akutem O_2-Mangel. *Pflüg. Arch. ges. Physiol.*, 1948, *250:* 79–90.

668. **Lalli, G.** Contributo allo studio di alcuni aspetti della funzione renale in anossia; comportamento della diuresi, della densita urinaria, dell'eliminazione dei solidi, dei cloruri de delle basi totali. *Riv. Med. aero., Roma,* 1950, *13:* 483–495. (English, French, Spanish, and German summaries.)

669. **McDonald, R. K. and V. C. Kelley.** Some observations of the effects of altitude anoxia on renal function. USAF. Randolph Field, Tex. School of aviation medicine. *Project 506, Rept. no. 1,* 6 January 1948, 8 pp. [P]

670. **Ochwadt, B.** Über Bicarbonatausscheidung und Kohlensäuresystem im Harn während akuter Hypoxie. *Pflüg. Arch. ges. Physiol.*, 1947, *249:* 452–469. [P]

10. REPRODUCTION

In general, decompression hypoxia depresses reproductive functions. According to Moore and Price (*675*) 1948, altitude levels greater than 14,260 feet are required to produce marked interference with the reproductive capacity of rodents when adequate nutritional states and temperature control are maintained. Altland (*671*) 1949 examined the

effects on growth and reproduction of discontinuous exposure of 247 rats to a simulated altitude of 24,000 feet for 4 hours daily. Growth was retarded in the exposed rats of both sexes, the reduction being greater in the male. The body weights of exposed male rats never attained more than 80 percent of the control weights, whereas the body weights of the exposed females reached control levels after 10 months. Exposure to altitude hypoxia did not affect the descent of the testis, but there was striking delay in the onset of sexual maturity. Spermatozoa were few in number as late as the 100th day of life. The vaginal orifice of exposed female rats opened 1 to 6 weeks later than litter-mate controls. Complete failure of breeding experiments presents evidence that the testis is unable to acclimatize to this degree of hypoxic stress. Histological examinations of ovaries gave evidence that ovulation had occurred in exposed female rats. Five pregnancies developed, but no living offspring were born. In a study of breeding performance in 131 rats exposed to 18,000 feet simulated altitude for 4 hours daily, Altland (*672*) 1949 found a significant reduction in the rate of reproduction in both sexes. In rats exposed only as adults, faulty gestation was observed. In those exposed from the 14th day of age there was a prevalence of implantation failure and early fetal death. Reproductive failures were also observed by Malmejac, Rossi, and Plane (*674*) 1950 in rats exposed to barometric pressures of 230 to 170 mm. Hg for 32 to 112 exposures at 4 hours each. After 60 exposures these animals did not reproduce until 10 months had elapsed. For further studies on reproduction abnormalities produced by hypoxia, papers by di Macco (*673*) 1946, Shettles (*676*) 1947, and Walton and Uruski (*677*) 1947 may be consulted.

671. Altland, P. D. Effect of discontinuous exposure to 25,000 feet simulated altitude on growth and reproduction of the albino rat. *J. exp. Zool.*, 1949, *110:* 1–16. [P]

672. Altland, P. D. Breeding performance of rats exposed repeatedly to 18,000 feet simulated altitude. *Physiol. Zool.*, 1949, *22:* 235–246.

673. Macco, G. di. Gonadi e ipossia. *Boll. Soc. ital. Biol. sper.*, 1946, *22:* 823.

674. Malmejac, J., M. Rossi, and P. Plane. Effets de séances répétées au caisson à dépression sur le comportement de "familles" de rats blancs. (Mus Decumanus, variété albinos.) *C. R. Soc. Biol., Paris*, 1950, *144:* 271–272. [P]

675. Moore, C. R. and D. Price. A study at high altitude of reproduction, growth, sexual maturity and organ weights. *J. exp. Zool.*, 1948, *108:* 171–216.

676. Shettles, L. B. Effects of low oxygen tension on fertility in adult male guinea pigs. *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 200.

677. Walton, A. and W. Uruski. The effects of low atmospheric pressure on the fertility of male rabbits. *J. exp. Biol.*, 1947, *23:* 71–76.

11. EFFECTS OF CARBON DIOXIDE ON HYPOXIA

The effects of adding carbon dioxide to the inspired air at lowered barometric pressures is discussed in the references given in this section. Certain favorable subjective and objective effects are reported. However, addition of carbon dioxide to respiratory mixtures as a means of improving altitude tolerance is probably not of practical value.

678. Garasenko, V. M. The use of carbon dioxide at lowered barometric pressures. *Amer. Rev. Soviet Med.*, 1944, *2:* 119–125.

679. Garasenko, V. M. The use of carbon dioxide at lowered barometric pressures. *Curr. Res. Anesth.*, 1945, *24:* 135–140. [P]

680. Hall, F. G. and K. D. Hall. Effect of adding carbon dioxide to inspired air on consciousness time of man at altitude. *Proc. Soc. exp. Biol., N. Y.*, 1951, *76:* 140–142. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1128. [P]

681. Langley, L. L., L. F. Nims, and R. W. Clarke. Role of carbon dioxide in the stress reaction to hypoxia. *Amer. J. Physiol.*, 1950, *161:* 331–335. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 412. Abstr.

682. Petrov, I. P. O znachenii uglekisloty pri kislorodnom golodanii. [Significance of carbon dioxide in oxygen deficiency.] pp. 184–200 in: *Kislorodnoe golodanie golognogo mozga; eksperimental'nye materialy.* [Oxygen deficiency of the cerebrum; experimental material.] Leningrad, Medgiz, 1949, 204 pp.

12. TOLERANCE

Various factors are known to affect tolerance to decompression hypoxia. For studies on the effects of diets and enzymes on tolerance, papers by the following authors should be consulted: Craven (*688*) 1950; Davis (*689*) 1948; Eckman, Barach, Fox, Rumsey, and Barach (*690*) 1945; Green, Butts, and Mulholland (*693*) 1945; Harris, Ivy, and Friedemann (*694*) 1947; Noell and Chinn (*700*) 1950; Riesen, Tahmisian, and Mackenzie (*704*) 1946; Seitz (*705*) 1942; Venturi (*707*) 1951; and Wolff and Karlin (*708*) 1947. In general, inanition results in an increase in tolerance. It also appears (*690*) that a high carbohydrate diet is attended by a greater tolerance than high fat or high fat protein meals. The gain in altitude tolerance with a high carbohydrate diet appears to be due to an increased respiratory quotient, a higher production of carbon dioxide with a given oxygen consumption, theoretically resulting in a proportionate rise in alveolar ventilation and oxygen tension. These findings have been confirmed by Green, Butts, and Mulholland (*693*) 1945 in human subjects. However, Noell and Chinn (*700*) 1950 found that intravenous glucose administration to rabbits did not affect the cerebral cortical survival time under conditions of anoxia as measured by cortical responsiveness to visual stimuli. Riesen,

Tahmisian, and Mackenzie (*704*) 1946 concluded that preflight administration of a single dose of glucose in water to individuals on a normal diet produced a significant increase in the resistance to unconsciousness from hypoxia at 27,000 feet and 30,000 feet. Protection afforded flying personnel by glucose administration was said to be greater 30 to 50 minutes following its administration than after an interval of 60 to 80 minues. Ascorbic acid, either alone or in conjunction with glucose, had no demonstrable effect on the duration of consciousness at altitude. The literature presents evidence that resistance to hypoxia may be enhanced by thiamine (*694*) and riboflavin (*694* and *708*), but not by methionine (*707*) or cytochrome C (*689*).

Investigations of drug prophylaxis against the lethal effects of hypoxia continue. Although some drugs can be shown to improve performance at low oxygen tensions, generally speaking, their use is dangerous and not of practical value. Investigations of pharmacological means for improving hypoxia tolerance are of great significance, however, in uncovering physiological and pathological effects of low oxygen tensions. The following recent reports should be consulted: Arnould and Lamarche (*683*) 1950; Barach, Eckman, Ginsburg, Johnson, and Brookes (*685*) 1946; Barmack, Woodruff, and Rossett (*686*) 1942; Burkhardt, Eastman, and Hale (*687*) 1950; Emerson, Morrison, and Van Liere (*691*) 1947; and Gardner and Forbes (*692*) 1945.

In studies of the effect of temperature on hypoxic failure in naval personnel in the altitude chamber, Houston, Cohen, Nuzie, and Bessen (*686*) 1944 and Houston, Nuzie, Seitz, and Bessen (*697*) 1944 found that at temperatures ranging from 84° to 98° F. at the incidence of hypoxic failure at 18,000 feet simulated altitude is slightly greater than in chilled runs at the same altitude. The severity of subjective complaints also increased with the increase in temperature.

The effect of age upon resistance to hypoxia has been reported by the following: Arshavski (*684*) 1945, Kolchinskaia (*699*) 1949, and Vail (*706*) 1946. These authors confirm the well-known fact that newborn animals are more resistant to hypoxia than adult animals.

Pace, Consolazio, and Lozner (*701*) 1945 have shown that polycythemia produced by transfusion of red blood cells in normal men affords increased tolerance to hypoxia. A group of 10 normal subjects were subjected to a simulated altitude of 15,500 feet. From the 14th to the 17th day of the experiment a total of 2,000 ml. of a 50-percent suspension in dextrose and saline of red cells from blood drawn less than 24 hours before was injected intravenously in each of the experimental subjects and a total of 2,000 ml. of dextrose and saline given to subjects in a control group. There was no increase in urinary pigment or hemoglobinuria. The oxygen capacity and arterial oxygen content of the blood increased significantly as a result of the transfusions. The arterial oxygen saturation at sea level and at altitude was unchanged by the transfusions. In the polycythemic period the pulse rate following exercise at low oxygen mixtures was significantly lower than the controls. The polycythemia persisted for approximately 6 weeks. There was no difference in the reticulocyte percentages of the two groups. From these studies, Pace, Lozner, Consolazio, Pitts, and Pecora (*702*) 1947 concluded that polycythemia induced artificially and polycythemia which occurs during acclimatization to high altitude are very similar. Therefore, the latter must play an important part in the attainment of acclimatization and may represent the bulk of the acclimatization process.

For other references to hypoxia tolerance, papers by the following may be consulted: Hiestand (*695*) 1946, Kline (*698*) 1947, and Pitts and Pace (*703*) 1947.

683. Arnould, P. and M. Lamarche. Action d'un antihistaminique de synthèse (2786 R. P. néo-antergan) sur la résistance du cobaye à l'anoxémie. *C. R. Soc. Biol., Paris,* 1950, *144:* 1088–1091.

684. Arshavski, A. Adaptation to anoxia at different age levels. *Amer. Rev. Soviet Med.,* 1945, *2:* 508–512.

685. Barach, A. L., M. Eckman, E. Ginsburg, A. E. Johnson, and R. D. Brookes. The effect of ammonium chloride on altitude tolerance. *J. Aviat. Med.,* 1946, *17:* 123–136. [P]

686. Barmack, J. E., J. L. Woodruff, and N. E. Rossett. The use of drug at high altitudes. The use of benzedrine and caffeine under conditions of oxygen want. City College of New York, Psychology laboratory, 9 July 1942, 17 pp. [P]

687. Burkhardt, W. L., B. R. Eastman, and H. B. Hale. Production of histamine in the body during hypoxia; influence of antihistaminics on respiratory response to hypoxia. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–24–015, Rept. no. 3,* July 1950, 4 pp. [P]

688. Craven, C. W. Effect of carrot feeding and starvation on the resistance of the rat to hypoxia. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–02–139,* March 1950, 10 pp. [P]

689. Davis, S. K. Effects of cytochrome C on anoxia. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command, ENG, Aero medical laboratory. Serial No. *MCREXD–696–112B,* 19 January 1948, 8 pp. [P]

690. Eckman, M., B. Barach, C. A. Fox, C. C. Rumsey, Jr., and A. L. Barach. Effect of diet on altitude tolerance *J. Aviat. Med.,* 1945, *16:* 328–340. [P]

691. Emerson, G. A., J. L. Morrison, and E. J. Van Liere. Drug prophylaxis against lethal effects of severe anoxia: IV. A stand technique. Influence of body weight, injection of saline, muscular restraint, rate of ascent, and

pre-treatment with oxygen or He–O_2 in anoxic mice. Report filed with U. S. NRC–CMR. 14 January 1947, 14 pp. [P]

692. **Gardner, T. S. and F. B. Forbes.** The effect of thiourea on mice undergoing an abrupt reduction of external atmospheric pressure. *J. Aviat. Med.*, 1945, *16:* 99–100. [P]

693. **Green, D. M., J. S. Butts, and H. F. Mulholland.** The relationship of anoxia susceptibility to diet. *J. Aviat. Med.*, 1945, *16:* 311–327. [P]

694. **Harris, S. C., A. C. Ivy, and T. E. Friedemann.** Work at high altitude. II. The effect of training and dietary restriction of thiamin and riboflavin on altitude tolerance and physical efficiency for work at a simulated altitude of 15,000 feet. *Quart. Bull. Nthwest. Univ.*, 1947, *21:* 135–151. [P]

695. **Hiestand, W. A.** A comparison of the effect of water starvation on anoxic death at ordinary barometric pressures with anoxic death caused by barometric decompression. *Anat. Rec.*, 1946, *94:* 420. Abstr. [P]

696. **Houston, C. S., E. J. Cohen, S. Nuzie, and G. E. Bessen.** Effect of temperature on anoxic failure in naval personnel in altitude chamber. U. S. Navy. Naval air station, Miami, Fla. Altitude training unit. *Project X–396, Rept. no. 1,* 27 January 1944, 2 pp. [P]

697. **Houston, C. S., S. Nuzie, C. P. Seitz, and G. E. Bessen.** Effect of temperature on anoxic failure in naval personnel in altitude chamber. U. S. Navy. Naval air station, Miami, Fla. Altitude training unit. *Project X–396, Rept. no. 2,* 8 August 1944, 4 pp. [P]

698. **Kline, R. F.** Increased tolerance to severe anoxia on carbon dioxide administration. *Amer. J. Physiol.*, 1947, *151:* 538–546. [P]

699. **Kolchinskaia, A. Z.** K voprosy o gipoksii tsentral'noi nervnoi sistemy. [Hypoxia of the central nervous system.] pp. 105–112 in: *Gipoksiia,* Kiev, Akad. Nauk. Ukr. SSR, 415 pp.

700. **Noell, W. K. and H. I. Chinn.** The effect of carbohydrates on cortical survival in anoxia. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–012, Final Rept.,* December 1950, 3 pp. [P]

701. **Pace, N., W. V. Consolazio, and E. L. Lozner.** The effect of transfusions of red blood cells on the hypoxia tolerance of normal men. *Science,* 1945, *102:* 589–591. [P]

702. **Pace, N., E. L. Lozner, W. V. Consolazio, G. C. Pitts, and L. J. Pecora.** The increase in hypoxia tolerance of normal men accompanying the polycythemia induced by transfusion of erythrocytes. *Amer. J. Physiol.*, 1947, *148:* 152–163. [P]

703. **Pitts, G. C. and N. Pace.** The effect of blood carboxyhemoglobin concentration on hypoxia tolerance. *Amer. J. Physiol.*, 1947, *148:* 139–151. [P]

704. **Riesen, A. H., T. N. Tahmisian, and C. G. Mackenzie.** Prolongation of consciousness in anoxia of high altitude by glucose. *Proc. Soc. exp. Biol., N. Y.*, 1946, *63:* 250–254. [P]

705. **Seitz, C. P.** Diet and tolerance to high altitude. City College of New York, Psychological laboratories, May 1942, 6 pp. [P]

706. **Vail', V. S.** Ohvliianii temperatury okruzhaiushchei sredy na vozrastnye kolebaniia chuvstvitel'nosti k kislorodnomu golodaniiu. [The effect of surrounding temperature on the sensitivity to oxygen deficiency in various age groups.] pp. 248–252 in: *Trudy Voenno-Meditsinskoi Akademii im. Kirova,* edited by L. A. Orbeli, N. N. Anichkova, I. P. Petrova, Moskva, A. V. Lebedinskogs, 1946, 269 pp.

707. **Venturi, V. M.** Azione della mentionina sulla resistenza all'ipossia sperimentale e sulla epatosi relativa. *Riv. Med. aero., Roma,* 1951, *14:* 650–654. (English, French, German, and Spanish summaries.) [P]

708. **Wolff, E. and R. Karlin.** La riboflavine hépatique et la résistance à l'anoxie chez la souris. *C. R. Soc. Biol., Paris,* 1947, *141:* 772–774. [P]

709. **Anon.** Glucose versus anoxia. *J. Amer. med. Ass.*, 1947, *133:* 776–777.

13. ACCLIMATIZATION

The references cited below represent a selection of the recent literature on acclimatization to decompression hypoxia. That adaptation to conditions of low oxygen does occur is well established. Under certain circumstances acclimatization can be lost. The physiological adaptations involved in acclimatization are complex and include cardiovascular, respiratory, hemotological, and other changes. One of the principal experimental investigations of acclimatization to high-altitude anoxia was "Operation Everest," carried out in 1946 at the U. S. Naval Air Station, Pensacola, Fla., School of Aviation Medicine. Reports of this study are given in references *719, 720, 721,* and *735.*

710. **Adams, W.** Acclimatization to intermittent anoxia. *J. clin. Invest.*, 1946, *25:* 912.

711. **Adams, W.** Acclimatization to intermittent anoxia. *J. clin. Invest.*, 1946, *25:* 912. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 185. Abstr.

712. **Adams, W. R., A. S. Alving, E. B. Bay, A. H. Bryan, H. T. Carmichael, T. J. Case, W. C. Halstead, M. Landowne, and H. T. Ricketts.** Effects of chronic intermittent anoxia in man: miscellaneous observations. U. S. NRC–CAM. *C. A. M. rept. no. 161,* 5 July 1943, 4 pp.

713. **Altland, P. D.** Effect of rest intervals on maintenance of previously induced high altitude acclimatization. *Fed. Proc. Amer. Soc. expt. Biol.*, 1949, *8:* 3–4.

714. **Altland, P. D. and B. Highman.** Acclimatization response of rats to discontinuous exposures to simulated high altitudes. *Amer. J. Physiol.*, 1951, *167:* 261–267. [P]

715. **Behnke, A. R., and S. W. Eyer.** Notes on the international symposium on high altitude biology—Lima, Peru. 23–30 November 1949, U. S. Navy. BuMed. 19 pp. [D]

716. **Clinton, M., Jr., G. W. Thorn, and V. D. Davenport.** Studies on altitude tolerance. II. Studies on normal human subjects—effect of repeated short exposures to reduced atmospheric pressure. *Johns Hopk. Hosp. Bull.*, 1946, *79:* 70–89.

717. **Dugal, L. P. and P. E. Fiset.** Sensibility of man to light anoxia. *J. Aviat. Med.*, 1950, *21:* 362–374 and 404.

718. **Grandjean, E.** L'adaptation de l'organisme humain à la montagne. *Schweiz. med. Wschr.*, 1949, *79:* 515–518.

719. **Graybiel, A., J. L. Patterson, and C. S. Houston.** The changes in heart size in man during partial acclimatization to simulated high altitudes. *J. Aviat. Med.*, 1951, *22:* 548–549. Abstr.

720. **Houston, C. S.** Operation Everest. A study of acclimatization to anoxia. *Nav. med. Bull., Wash.*, 1946, *46:* 1783–1792. [P]

721. Houston, C. S. The adaptations which produce acclimatization to oxygen lack. *J. Aviat. Med.*, 1947, *18:* 237–243. [R]

722. Ivanov, I. I. The mechanism of adaptation of animals to low partial oxygen pressures. *C. R. Acad. Sci., U. S. S. R.*, 1946, *51:* 613–614. [P]

723. Jéquier-Doge, E. À propos du déficit-oxygène. *Schweiz. med. Wschr.*, 1950, *80:* 587–593. [D]

724. Lipin, J. L. and W. V. Whitehorn. Role of metabolism in the acclimatization of albino rats to reduced barometric pressure. *J. Aviat. Med.*, 1950, *21:* 405–413.

725. McDonald, R. K. and V. C. Kelley. Study of acclimatization during a two-week exposure to moderate altitude. Some observations on the effects of altitude on metabolism. III. Hemoglobin metabolism and erythropoiesis. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–02–029, Rept. no. 3,* October 1949, 10 pp. [P]

726. Opitz, E. Increased vascularization of the tissue due to acclimatization to high altitude and its significance for the oxygen transport. *Exp. Med. and Surg.*, 1951, *9:* 389–403. [P]

727. Opitz, E. and F. Palme. Darstellung der Höhenanpassung im Gebirge durch Sauerstoffmangel. II. Atmung und kritische alveolare Sauerstoffspannung bei Rückatmung im Gebirge. *Pflüg. Arch. ges. Physiol.*, 1944, *248:* 298–329. [P]

728. Opitz, E. and F. Palme. Sauerstoffmangel zur Darstellung der Akklimatization im Gebirge. V. Abflachung von T in Elektrokardiogramm. *Pflüg. Arch. ges. Physiol.*, 1944, *248:* 387–404. [P]

729. Poel, W. E. Effect of anoxic anoxia on myoglobin concentration in striated muscle. *Amer. J. Physiol.*, 1949, *156:* 44–51.

730. Rahn, H. and A. B. Otis. Man's respiratory response during acclimatization to high altitude. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 96–97.

731. Reynolds, O. E. and N. E. Phillips. Adaptation of the albino rat to discontinuous chronic exposure to altitude anoxia. *Amer. J. Physiol.*, 1947, *151:* 147–154. [P]

732. Rose, H. W. Study of acclimatization during a two-week exposure to moderate altitude (10,000 feet). Effect of altitude adaptation on night vision and ocular muscle balance. USAF. Randolph Field, Texas. School of aviation medicine. *Project 21–02–029, Rept. no. 1,* March 1949, 16 pp. [P]

733. Sanboz, L. M. Quelques aspects de l'adaptation à l'altitude. *Méd. aeronaut.*, 1950, *5:* 94. (French abstract). *Gesdh. Wohlfahrt, Schweiz*, 1947, *27:* 349–366.

734. Thorn, G. W., M. Clinton, Jr., S. Farber, and H. W. Edmonds. Studies on altitude tolerance. 1. Studies on normal rats—effect of repeated short exposures to reduced atmospheric pressure. *Johns Hopk. Hosp. Bull.*, 1946, *79:* 59–69.

735. U. S. Navy. School of aviation medicine. NAS, Pensacola, Fla., Operation Everest. 1946, 38 pp.

736. Van Liere, E. J. Acclimatixation, pp. 140–158, in: *Anoxia. Its effect on the body.* Chicago, The University of Chicago Press, 1942, 269 pp.

737. Van Middlesworth, L. Acute adaptation of rats to very low oxygen pressure. *Proc. Soc. exp. Biol., N. Y.*, 1949, *72:* 476–478. [P]

738. Wilhelm, R. E., M. S. Comess, and J. P. Marbarger. Performance under acute hypoxic stress in acclimatized mice. *J. Aviat. Med.*, 1950, *21:* 313–317. [P]

739. Wyss, F. and A. Gianoli. Die Veränderung der Kapillarresistenz im Höhenklima. *Schweiz. med. Wschr.*, 1946, *76:* 626–630. [P]

740. Zoll, M. *Contribution à l'étude de l'adaptation à l'altitude. Les réactions d'acclimatement après des sejours successifs en caisson à dépression.* Travail du Centre d'Etudes de Biologie Aeronautique du service de Santé de l'Air. Dijon France, 1949, 64 pp. [R] [P]

IV. PHYSIOLOGICAL EFFECTS OF HIGH CARBON DIOXIDE CONTENT IN ENVIRONMENTAL AIR

A. GENERAL STUDIES

The existing literature on the physiological effects of high carbon dioxide concentration in environmental air gives extensive and valuable information on the acute and subacute effects of carbon dioxide upon man and animals. Although this information is valuable from a comparative as well as human standpoint, nevertheless there are significant defects in our understanding of the actions of high concentrations of high carbon dioxide over prolonged periods of time. Long submergence in submarines imposes the hazard of intolerable concentrations of carbon dioxide and it becomes important to have accurate information on the limits of carbon dioxide tolerance under conditions of actual operations over long periods. Animal studies cannot be uncritically applied to the human situation and even dockside tests simulating periods of prolonged submergence do not fully reproduce the actual stresses of combat situations. A further difficulty is imposed by the problem of measuring accurately the limits to tolerance in terms of performance breakdown.

In the present section, papers by the following authors are particularly valuable in affording a comprehensive review of the physiological effects of high carbon dioxide content in the environmental air: Consolazio, Fisher, Pace, Pecora, Pitts, and Behnke (*743*) 1947; Fenn (*746*) 1948; MacIntosh (*748*) 1946; Schaefer (*749* and *750*) 1951; and Schäfer, Storr, and Scheer (*751*) 1949.

741. Anselmo, J. E., D. E. Pesigan, G. D. Dizon, V. J. Luciano, and J. Y. Navarro. Fatal poisoning from carbon dioxide. Report of five cases with two deaths. *J. Phil. Is. med. Ass.*, 1951, *27:* 102–105. [CH]

742. Chapin, J. L. *The ventilatory response to, toxicity of, and acclimatization to carbon dioxide.* Thesis (Physiol.), University of Rochester, Rochester, New York. 1949, 164 pp. [P]

743. Consolazio, W. V., M. B. Fisher, N. Pace, L. J. Pecora, G. C. Pitts, and A. R. Behnke. Effects on man of high concentrations of carbon dioxide in relation to various oxygen pressures during exposures as long as 72 hours. *Amer. J. Physiol.*, 1947, *151:* 479–503.

744. Cordier, D. and J. Chanel. Influence de la tension de l'anhydride carbonique dans l'air inspiré sur la vitesse

de l'absorption intestinale des solutions isotoniques de glucose chez le rat. *J. Physiol., Paris,* 1950, *42:* 459–462.

745. Doro, B. Un case di asfissia in uncilindro di spinta. *Rass. Med. indust.,* 1949, *18:* 67–74.

746. Fenn, W. O. Physiology of exposures to abnormal concentrations of the respiratory gases. *Proc. Amer. phil. Soc.,* 1948, *92:* 144–154. [R]

747. Lvovich, D. B. [Accident in a well with great concentration of carbon dioxide.] *Gigiena San., Moskva,* 1951, *7:* 50–51.

748. MacIntosh, F. C. Partial pressure of CO_2 in flooded submarine compartments. Gt. Brit. MRC–RNPRC. Prepared for Admiralty Committee on Submarine Escape. *R. N. P. 46/285,* May 1946, 12 pp. [P]

749. Schaefer, K. E. Chronic carbon dioxide toxicity. *Amer. J. Physiol.,* 1951, *167:* 823–824.

750. Schaefer, K. E. Studies of carbon dioxide toxicity (1) Chronic carbon dioxide toxicity in submarine medicine. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 015.03.05,* 21 August 1951, 20 pp. [R]

751. Schäfer, K. E., H. Storr, and K. Scheer. Über langdauernde Einwirkung verschieden höher CO_2—Konzentrationen auf Meerschweinchen. *Pflüg. Arch. ges. Physiol.,* 1949, *251:* 741–764. [P]

752. U. S. Navy. Memorandum from Force Medical Officer, COMNAVGER to Intelligence Officer, COMNAVGER. Medical visit to French submarine and underwater research units. 12 December 1951, 4 pp.

B. NERVOUS SYSTEM

Lorente de No (*767*) 1947 has presented an analysis of the effect of carbon dioxide upon membrane potential and upon the functional ability of frog nerve. Carbon dioxide increases the membrane potential and it is this increase that raises the threshold of stimulation and decreases the speed of conduction as well as increases the height of the response. It appears that the effect of carbon dioxide upon the nerve progressively decreases with increasing length of time of survival. Carbon dioxide also increases the negative after potential following the supernormal phase. The membrane potential of a nerve kept in an atmosphere of 95 percent oxygen and 5 percent carbon dioxide is the sum of 2 fractions. One fraction is restored at a slow rate after conduction of impulses and consequently disappears during tetanic stimulations of frequencies above 60 per second. This is called the L- (labile) fraction while the other fraction is larger and is restored with greater rapidity during the descending phase of the spike. For this reason this fraction is called the Q- (quick) fraction. During restoration of a potassium-treated nerve by the action of 5 percent CO_2, the membrane potential is increased by an amount somewhat greater than the height of the negative afterpotential produced by short tetani at moderate frequency. This difference is the increment of the Q-fraction and experimental observations indicate that this increment is the direct cause of the relief of the potassium block. It can be said that the presence of 5 percent carbon dioxide increases the ability of the nerve to perform work, undoubtedly because the enzymatic mechanisms of the nerve utilize stores of metabolic energy more rapidly or more effectively in the presence than in the absence of a certain concentration of carbon dioxide. The author believes that CO_2 acts upon the nerve by participating in reactions of the oxidative metabolism. It results in an increase of the membrane potential since the presence of carbon dioxide displaces the point of equilibrium of respiratory reactions.

In a study on five subjects who underwent a 6-day exposure to an atmosphere containing 3 percent carbon dioxide, Schafer (*775*) 1949 measured their excitation time at the motor point (nerve point) of the brachiordalis muscle during exposure. Strength-duration curves were plotted and the chronaxie values obtained by extrapolation. Continuous respiration of a 3-percent carbon dioxide-air mixture was found to have an exciting influence on the men in the first 24 hours, and a contrary effect in the following period. During the first and most of the second day of the exposure period, the chronaxie and simultaneously the rheobase were found to be decreased. From the third day onwards, the chronaxie and rheobase were increased to twice the control value. The author concluded that the changes in chronaxie and rheobase during acute and chronic exposure to 3 percent carbon dioxide are due to an acceleration followed by a retardation of the processes underlying excitation of the nerves.

Early effects of carbon dioxide excess on spinal reflexes have been reported by Kirstein (*763*) 1951. In these studies, cats, decapitated by spinal section, were maintained by artificial respiration. The ventral roots T_7 and S_1 were cut and reflex discharges recorded by a five-stage condenser-coupled amplifier and a cathode-ray oscillograph. The effects of breathing nitrogen or breathing a mixture of 8.9 percent carbon dioxide and 91.1 percent oxygen were determined. Studies were also made of the effects of clamping the aorta. After 20 seconds of breathing nitrogen, the monosynaptic extensor reflex was diminished in amplitude to 60 percent. Eighty seconds later the amplitude increased to 190 percent, and finally after another 30 seconds the height of the reflex discharge decreased to 30 percent. As for the polysynaptic reflex there was no change in the first 20 seconds, but after 30 seconds there was an increase up to 140 percent followed by a gradual decrease. Aortic occlusion led to an immediate or early 35 percent decrease in the monosynaptic extensor reflex followed by augmentation

after 15 seconds up to 300 percent and then a decrease after 60 seconds. In animals breathing nitrogen and anesthetized with Dial there was no initial depressive stage in the monosynaptic reflexes, but an increase of 120 percent was noted. Breathing the carbon dioxide mixture resulted in a gradual diminution of the monosynaptic reflex to 40 percent in 4 minutes. With the polysynaptic reflex no change was observed in the first minute, with a decrease of 20 percent in 2 to 3 minutes. Thus the depressant action of carbon dioxide is confirmed as spinal in origin. In similar studies of submaximal two-neuron arc responses resulting from medial popliteal nerve stimulation, Bradley, Schlapp, and Spaccerelli (*755*) 1950 found that carbon dioxide in the inspired air in amounts from 0.5 to 9 percent produced only depression of the response. The effects were not due to hypoxia or blood-pressure changes. Lactic acid injected intravenously in amounts sufficient to produce equivalent blood pH changes did not have a similar effect. Carbon dioxide did not increase the inhibition resulting from conditioning shocks applied to the lateral popliteral nerve.

For a definitive and authoritative report on the action of carbon dioxide on the respiratory centers and other neurological mechanisms, a paper by Brazier (*756*) 1943 should be consulted. This paper contains an excellent review of the literature and comprises approximately 300 references. The author has discussed the mechanisms by which carbon dioxide combats the effects of hypoxia through increase in respiratory volume due to direct stimulation of the respiratory centers; by a shift in the oxygen dissociation curve of blood so that oxygen is released more rapidly to the tissues; and through increase in the blood flow through the brain (by the action of carbon dioxide on cerebral vessels), increased sensitivity of vasomotor centers, reflex stimulation of the carotid and aortic bodies, and augmentation in the rise of blood pressure caused by hypoxia, improved venous return by the vasopressor effect of carbon dioxide, and the mechanical effects on the veins by respiratory pumping also play a role.

On the subject of the specific action of carbon dioxide on the respiratory center, Leusen (*765*) 1951 found that in dogs under morphine-chloralose anesthesia after vagosympathetic section and isolation of the carotid sinuses, perfusion of cerebral ventricles with solutions at various pH values, obtained by adding carbon dioxide led to respiratory stimulation at low pH and respiratory depression at high pH. When solutions without sodium bicarbonate were used at pH values between 6.5 and 7.8, the changes in pH did not produce variations in respiratory activity. When sodium bicarbonate was added, a change of 0.3 pH unit produced a change in the central stimulation effect. According to Beyne, Chauchard, and Chauchard (*753* and *754*) 1947, a minimal degree of carbon dioxide excess has a depressant effect upon the central nervous system. Measurement of chronaxie permits early detection of this narcotic effect of carbon dioxide before it becomes clinically manifest. Small doses of carbon dioxide produce this depressant action preceded by an excitation, indicated by an early diminution of chronaxie. There is a difference in sensitivity between the cerebrum, which is excited only transiently by small doses, and the respiratory center, which continues to be excited by large doses. In the authors' studies, the carbon dioxide percentages ranged from 0.25 percent to 3 percent. According to Heymans and Pannier (*761*) 1948, diminution of pressure at the level of the carotid sinus in dogs results in a hyperpnea while breathing air. This hyperpnea persisted for some time in spite of acapnia. The hyperpnea initiated by inhalation of carbon dioxide is pronounced when the pressure at the level of the carotid sinus is maintained above the normal level.

Regarding the action of carbon dioxide on the excitability of sympathetic reflexes, Thieblot and Guilhem (*780*) 1946 found that dogs subjected to 3 to 8 percent carbon dioxide in air showed an increase in the reflex excitability of the sympathetic vasomotor center and an increase of time of summation measured in the hypogastric and splanchnic nerves. Carbon dioxide was found to be a weak mydriatic in dogs under chloralose anesthesia by Hoorens (*762*) 1948.

The central action of carbon dioxide has also been investigated in studies of its effects upon cold shivering. Hensel (*760*) 1949 found that at a room temperature of 10° C. in normal air, cold shivering was produced only in predisposed subjects. Air containing 3 percent carbon dioxide elicited cold shivering in all experimental persons. This carbon dioxide effect was enhanced by either hyperventilation with carbon dioxide or by increasing the carbon dioxide content of the air breathed by as little as 0.2 percent. Cold shivering was held to be produced centrally.

The central inhibitory effects of carbon dioxide have been studied by Pollock and associates (*758, 773, 774,* and *778*). In cats Pollock (*773*) 1949 found that high concentrations of carbon dioxide in oxygen increase the frequency, but lowers the amplitude of the electroencephalographic waves. Carbon dioxide was found to antagonize seizures induced by

metrazol and by electricity. It was found that 30 percent carbon dioxide is more effective than 20 percent. The 20 percent mixture is more effective than a 15 percent mixture and so on down through different dilutions to a 5-percent carbon dioxide mixture. The antagonism is present in low and high partial pressures of oxygen. Hyperventilation and breathing of pure oxygen seem to enhance the convulsive response to electric shock, whereas low oxygen (6 percent) and 100 percent nitrogen produce antagonism to seizure activity. The duration of administration of the carbon dioxide mixtures and the strength of stimulus applied appear to be important factors in addition to the concentration of carbon dioxide. Utilizing the techniques described, it was found that the cerebellum did not respond with seizures to electrical stimulation. Stein and Pollock (*778*) 1949 found that concentrations of carbon dioxide over 20 percent prevented seizures due to electric stimulation when the mixture was inhaled for 3 minutes. The animals used in these studies were monkeys (Macacus rhesus). In a study on patients, Pollock, Stein, and Gyarfas (*774*) 1949 produced seizures by stimulation with suprathreshold shocking current. It was found that concentrations of carbon dioxide from 15 to 30 percent routinely prevented electrically induced seizures. With 30 percent carbon dioxide, 30 seconds of inhalation sufficed, whereas with 15 to 20 percent mixtures, slightly longer periods of time were required. Gyarfas, Pollock, and Stein (*758*) 1949 found that inhalation of 30 percent carbon dioxide and 70 percent oxygen in human subjects produced in all cases convulsive phenomena. There was initial periocular twitching followed by either an extensor hypertonus in all extremities or, more often, slight flexor spasms in the arms and extension in the legs, consecutive transitory plastic tonus, increasing occipital rigidity and opisthotonus, and finally a high degree of extensor rigidity in all the limbs. The fingers were in the "main d'accoucheur" position and the toes were in flexion. The dilated pupils reacted to light on most occasions. The tendon and skin reflexes could not be elicited on account of the muscular rigidity. Pathological reflexes were not seen during or after the convulsion, though in some cases they preceded them. There was no biting of the tongue, incontinence, or postconvulsive stupor. The electroencephalogram, though obscured by muscular movements, was stated always to be clearly not of the grand mal type. The electrical activity of the cortex returned to normal shortly after discontinuing inhalation of carbon dioxide. The clinical symptoms, the electroencephalogram, and the absence of postseizure stupor, correspond to decerebrate seizures. Seizures produced by breathing high carbon dioxide concentrations in both animals and man have been described by Meduna (*768, 769*) 1950.

Moussatche (*772*) 1951 found that carbon dioxide in high concentrations produced convulsions in rabbits, but not in the hind limbs after thoracic spinal cord section. Convulsions produced in morphinized dogs by application of strychnine or acetylcholine to the cerebral cortex were inhibited by breathing high carbon dioxide mixtures. The tension required for inhibition being less (12 to 20 percent) for cortical than for spinal convulsions. Tension of carbon dioxide required to suppress spinal-cord convulsions induced by injected strychnine was the same in spinal cord sectioned as in intact rabbits. Deafferentation of aortic arch and carotid sinus had no effect on the carbon dioxide level required for anticonvulsive effects. The action of carbon dioxide in these situations is evidently directly upon the centers. The mechanism of the inhibitory action of carbon dioxide has also been studied by Moussatche (*771*) 1950 on frogs in which it was shown that breathing a mixture of atmospheric air containing 30 percent carbon dioxide for 20 minutes abolished attacks of cryoepilepsy. Frogs subjected to concentrations of carbon dioxide above threshold necessary to prevent attacks of cryoepilepsy did not show depression of the pH of the blood to values lower than those obtained with perfusion of acidified Ringer's solution. It was concluded by the author that the fall in pH is not the cause of inhibition by carbon dioxide of the cryoepilepsy. Changes in the brain pH response to carbon dioxide after prolonged hypoxic hypoventilation have been reported by Brown (*757*) 1950. Carbon dioxide titration curves of brain homogenate were determined for guinea pigs. A given carbon dioxide tension produced a lower pH in the brain homogenates of the hyperventilated animals than in the controls, and it was suggested that this reduction in the buffering ability of the brain for carbon dioxide following prolonged hyperventilation may be the mechanism by which increased sensitivity of the respiratory center to carbon dioxide following such prolonged stress is brought about.

For discussions of the effects of carbon dioxide upon cerebral functioning, several references may be consulted (*766, 770, 776, 777, 779*). Schafer (*776*) 1949 has described the effects of concentrations of 2 to 5 percent CO_2 upon brain action. The depression phase of carbon dioxide was expressed in two findings: (1) disappearance of the hypercapnia effect after 3 days exposure to 3 percent

carbon dioxide, and (2) disappearance of the normal inhibitory effect of sensory stimuli on the brain action potentials after 3 days in 3 percent carbon dioxide. This disappearance of the normal inhibitory effect of sensory stimuli was found to develop parallel with a general decrease of the excitability of the respiratory center. Observations on psychoneurotic patients made by Meduna and Gyarfas (*770*) 1949 draw attention to widespread alterations of nervous activity ranging from primordial sensory phenomena to complicated dreams with or without emotional discharge, short temporary states of confusion, hallucinations, and complicated cortical or subcortical discharges. It was concluded that therapeutic administration of carbon dioxide produces decreased function of inhibitory cortical areas. Why this is of benefit in therapy can only be answered when there is an adequate physiological theory of the neuroses. Liest (*766*) 1949 has also reported personality mutation following carbon dioxide inhalation. This author believes that carbon dioxide has its effects in descending order on (1) the cortex, (2) the basal ganglia and subcortical structures, (3) the cerebellum, (4) sensory areas of the cord, (5) motor areas of the cord, and (6) the medulla. Side reactions of carbon dioxide were manifested in sensory, motor, psychosensory, and psychomotor changes. Carbon dioxide differs from other exogenous agents by the fact that it is in itself a powerful physiological agent in the regulation of intracranial metabolism. The author attributes the therapeutic effect of carbon dioxide inhalation to retrogressive, functional suppression of those cerebral structures of specific gnosi-discriminative utility. He states that the inhalation of carbon dioxide is inhibitive, paralytic, and, broadly speaking, dyscratic rather than stimulative in its pharmacological action.

The effects of carbon dioxide upon the perception of thermal cutaneous pain have been studied by Stokes (*779*) 1948 who found that carbon dioxide can produce specific analgesia. He considers that the analgesic effect of carbon dioxide is not peripheral, but mainly central. According to Simonson and Winchell (*777*) 1951, a mixture of 5 percent carbon dioxide and 95 percent oxygen in normal healthy subjects caused a significant drop of fusion frequency of flicker within 12 minutes. The drop was faster and greater with the carbon dioxide mixture than with an air mixture containing 14 percent oxygen and 86 percent nitrogen. For a report on confusion, dizziness, and headache from exposure to high concentrations of carbon dioxide (4 to 9 percent) subsequently breathing oxygen or normal air, a paper by Hayter and Duffner (*759*) 1948 should be consulted.

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C. HEART AND CIRCULATION

The effect of increased carbon dioxide on respiration and heart rate of hibernating hamsters and ground squirrels has been investigated by Lyman (*799*) 1951. The respiratory rate of deeply hibernating hamsters and ground squirrels was increased by concentrations of carbon dioxide above 2.5 percent. The heart rate of ground squirrels usually increased with the respiratory rate, but concentrations of carbon dioxide above 5 percent were necessary to increase the heart rate of hamsters. Ground squirrels remained in hibernation in spite of the higher heart rate, but the more easily aroused hamsters would waken if exposed for more than a few minutes to concentrations of carbon dioxide higher than 5 percent. It was concluded by the author that these rodents in the hibernating state retain homeostatic respiratory and cardiac mechanisms in spite of their low body temperature and apparently insensitive condition.

Regarding the effect of breathing carbon dioxide on the output of the heart, Asmussen (*783*) 1943 showed in human subjects that hyperventilation caused by carbon dioxide breathing has an increased effect on the cardiac output if the subject lies horizontally. There is no effect, however, if the subject is tilted to an upright position. The author concluded that the effect of carbon dioxide breathing on the cardiac output must be due to the mechanical forces of hyperventilation and not to a chemical action of carbon dioxide on the circulation, as otherwise the difference of the effect in the two positions is unexplained.

Meeter (*801* and *802*) 1948 found in dogs under chloralose anesthesia with both vagii cut that breathing 10 percent carbon dioxide resulted in a considerable reduction of oxygen consumption. The cardiac output decreased with oxygen consumption, but the heart rate did not change in these experiments. Dilatation of the heart under carbon dioxide was striking, but was reversible. With metabolic decrease there was a reduction of stroke volume. The author found the pacemaker of the heart very insensitive to carbon dioxide. In a series of dogs inhaling an air mixture containing 5 percent carbon dioxide, 21 percent oxygen, and 74 percent nitrogen, Patterson, Waits, and McPhaul (*805*) 1951 found that the cardiac output either fell slightly or was unchanged. In chloralosed dogs not given tetraethylammonium chloride, carbon dioxide regularly produced a rise in mean arterial blood pressure and a fall in limb flow of 6 to 50 percent. In animals given tetraethylammonium chloride, there was a fall in arterial blood pressure of 4 to 23 mm. Hg and a rise in limb flow of 8 to 84 percent. In these latter cases, the cardiac output usually fell moderately. These studies suggested to the authors that the direct action of carbon dioxide and that mediated by nervous mechanisms are in competition. The fall in cardiac output with an associated rise in limb flow suggested that the direct dilatory effect of carbon dioxide on limb vessels must not be representative of the entire vascular system. In these studies tetraethylammonium chloride was given in dosages sufficient to cause complete ganglionic blockade.

Regarding changes in the electrocardiogram, Altschule and Sulzbach (*782*) 1947 found that breathing of a mixture of 5 percent carbon dioxide and 95 percent oxygen in man resulted in a lowering of the arterial blood pH to about 6.9 with changes in the electrocardiogram indicative of

myocardial damage. These changes were rapidly reversible after cessation of each experiment and decreased in severity when the experiments were repeated several times in the same patient. The authors concluded that the human myocardium, although more tolerant to acidosis than was previously believed, appears to be less tolerant than the canine heart. Christensen (*787*) 1946 recorded electrocardiographic signs of myocardial hypoxemia in normal human subjects hyperventilating voluntarily. Continued hyperventilation of a mixture of 5 percent carbon dioxide, 20 percent oxygen, and 75 percent nitrogen resulted in a disappearance of the electrocardiographic changes in less than 1 minute. It was suppposed that the changes are due to acapnia and alkalosis. On the basis of animal experiments, the authors concluded that myocardical hypoxemia may be caused either by constriction of the coronary vessels or increased intramyocardial tension, or a combination of the two. Large doses of nitroglycerin given immediately before the experiment did not prevent the occurrence of the hypoxemic electrocardiographic changes. It was therefore concluded that they were not caused by coronary constriction alone, but were due chiefly to an increase intramyocardial tension.

In studies on dogs, Spencer, Parry, Whitehead, and Draper (*807*) 1950 gave carbon dioxide percentages of 10, 20, 30, and 40 percent to animals under thiopental sodium anesthesia. The venous blood pH was depressed roughly proportional to the carbon dioxide concentration in an amount approximating 0.2 of a unit for each increment of 10 percent in carbon dioxide concentration. A marked increase in amplitude of the T-wave occurred, but there was no correlation between the amount of elevation of the T-wave and the concentration of carbon dioxide inhaled.

For studies on the effect of intravenous injections of carbon dioxide upon the electrocardiogram of dogs, papers by the following should be consulted: Durant, Long, and Oppenheimer (*788*) 1948; Durant, Long, Oppenheimer, and Wester (*789*) 1947; and Durant, Long, and Oppenheimer (*793*) 1947. In these studies, dogs under barbiturate anesthesia were used. The chest was opened and the animal was ventilated through a tracheal canula. Fifty cu. cm. of carbon dioxide were rapidly injected into the femoral vein. The gas was collected in the right ventricle, preventing the passage of blood into the lungs. The right heart was found to dilate and the blood pressure fell. The initial "up" deflection was found to disappear entirely in the direct lead. Injections of carbon dioxide of 10 to 15 cu. cm. resulted in lowering of the R-wave, while with 50 cu. cm. or more of carbon dioxide the R-wave disappeared entirely. The decrease in amplitude of the R-wave was proportional in the amount of carbon dioxide injected. The P-wave was increased in amplitude and the ST segment raised. The T-wave was inverted. When 30 cu. cm. of 1 percent procaine was injected, the QRS interval increased, and when the action of carbon dioxide was superimposed upon that of procaine, the pattern from the surface of the right ventricle resembled that of right bundle-branch block. Breathing gas mixtures containing 4 to 10 percent carbon dioxide in acute experiments in human subjects results in a rise in diastolic and systolic arterial blood pressure.

Alella and Meda (*781*) 1948 exposed men to a gas mixture containing up to 4.7 percent carbon dioxide and 20 percent oxygen. In these studies the pulse rate was increased as well as diastolic, systolic, and mean arterial blood pressures and the minute volume. There was a decrease in peripheral resistance. In human subjects breathing various oxygen-nitrogen mixtures, Penneys (*806*) 1950 found that changing to 5 percent carbon dioxide in nitrogen and oxygen or 5 percent carbon dioxide in oxygen allayed symptoms in all cases. Both systolic and diastolic arterial blood pressures were consistently higher with carbon dioxide in the gas mixtures, especially at 70 percent arterial saturation. In no cases was there so great an elevation in arterial blood pressure as to warrant termination of the test. The highest was 150 mm. Hg systolic pressure. Mayerson (*800*) 1946 has investigated the use of carbon dioxide in preventing postexercise orthostatic circulatory insufficiency. This author has called attention to the fact that many subjects faint when kept motionless in the upright position after performing a standard amount of moderate exercise. The postexercise response of these subjects is particularly characterized by a low and rapidly falling systolic blood pressure and circulatory failure within 5 to 10 minutes after the exercise is finished. In the author's study, 10 such "fainters" were made to breathe air containing from 4 to 10 percent carbon dioxide for varying intervals after exercise. When carbon dioxide was given immediately after exercise, the postexercise systolic blood pressure level was high and dropped only gradually. Syncope did not occur and the pattern of response resembled that of the "nonfainter." Also the administration of carbon dioxide when syncope was imminent resulted in a reversal of the pattern of response and averted the collapse. Respiratory gas analyses indicated that

the carbon dioxide content of the alveolar air in "fainters" is diminished after the exercise and remains from 25 to 40 percent lower than the pre-exercise level, whereas the drop in "nonfainters" is less (5 to 25 percent). The author suggested that under the conditions of his experiments the level of carbon dioxide in the "fainters" fell below that necessary to stimulate the vasomoter center, and that the rise in systolic blood pressure following the administration of carbon dioxide is due to stimulation of the vasomotor center and a consequent vasoconstriction which counteracts the local dilatation produced during exercise. Little, Avera, and Hoobler (*798*) 1949 found a rise of 21 percent in the mean arterial blood pressure in normotensive subjects and 16 percent in hypertensive subjects during inhalation of a gas mixture containing 10 percent carbon dioxide and 90 percent oxygen. The authors ascribed this rise in part to increased vasomotor tone, but also in part to an increase in cardiac output, since it also occurred after caudal anesthesia had been established to the third dorsal segment. The procedure also resulted in a reduction of renal plasma flow and an increase in renal resistance. These changes were greater in the hypertensive than in the normotensive group.

Gibbs, Maxwell, and Gibbs (*790*) 1946 and (*791*) 1947 have studied the volume flow of blood through the brain of man at rest, during hyperventilation, and while breathing high concentrations of carbon dioxide. In the authors' studies an 0.2 percent solution of Evan's Blue (T–1824) was injected into the right internal carotid artery of human patients at a rate of 1 cu. cm. per minute. Blood samples were drawn from the right internal jugular vein with or without occlusion of the left internal jugular vein, while simultaneous arterial samples were obtained from the femoral artery. The rate of injection and the difference in concentration of the dye in the arterial and venous samples gave the necessary information for estimating cerebral blood flow. With this value and the arteriovenous differences for oxygen it was possible to estimate oxygen consumption. This method was checked in one case against direct volumetric determinations of cerebral blood flow. The average resting blood flow for all subjects was found to be 617 cu. cm. per minute and the average oxygen consumption was 39.2 cu. cm. per minute. Hyperventilation reduced the cerebral blood flow to approximately one-half the control level. By breathing 10 percent carbon dioxide it was possible to double the cerebral blood flow. Changes in arteriovenous differences for oxygen were in the same direction and of the same general magnitude as were to be expected from the changes in blood flow.

The literature indicates that in acute experiments breathing of high concentrations of carbon dioxide in animals results in pulmonary vasoconstriction and rise of pulmonary arterial blood pressure. In the isolated perfused lungs of monkeys (Macacus rhesus), Hebb and Nimmo-Smith (*794*) 1948 found that inhalation of carbon dioxide in relatively large amounts led to a rapid rise in pulmonary arterial blood pressure which was considered to be due to constriction of pulmonary vessels. These authors did not see this effect when similar tests were made on isolated perfused lungs of dogs. However, Duke (*792*) 1949 exposed isolated dogs' lungs to 5 and 10 percent carbon dioxide in air, and noted a diminution in the capacity of the pulmonary blood vessels and a 5 to 20 percent increase in pulmonary arterial blood pressure. The lung volume showed an inverse relationship to the carbon dioxide content of the arterial blood. The effect of adrenaline on pulmonary vessels was not altered during ventilation of the lungs with 5 percent carbon dioxide, and the response also was not inhibited by ergotoxine or by atropine. In isolated and perfused lungs of the cat, Nisell (*804*) 1948 found that inhalation of 6.5 percent carbon dioxide in oxygen increased the pulmonary blood pressure. The author considered that the response was due to a direct effect of carbon dioxide on pulmonary blood vessels. Van Euler and Liljestrand (*808*) 1946 found in cats that breathing 6.5 percent carbon dioxide in oxygen resulted in a moderate increase in pulmonary arterial blood pressure. Tests with higher carbon dioxide concentrations gave the same result.

In isolated dog lungs perfused with heparinized dog blood under constant pressure, Bean, Mayo, O'Donnell, and Gray (*784*) 1951 found that shifting from normal blood to high carbon dioxide blood for short periods resulted in a reversible decrease in outflow of blood from the ventilated and quiescent lung. This response was occasionally preceded by an initial light increase and not infrequently followed by a late tendency to an increase in flow. The authors concluded that the effect of carbon dioxide was to increase the resistance to outflow of blood as a consequence of a constrictive action of carbon dioxide on effluent vessels or on parenchymal smooth muscle and a passive or active dilatation of blood reservoir regions of the lung. Air was expelled from the lung as a result of the constrictive effect of carbon dioxide on the smooth muscle of the bronchial tree and to some extent also to an encroachment of distended blood reservoirs upon the alveolar air volume. Shift to high carbon dioxide also caused a

predominant decrease of inflow of blood to the lung, following an initial transient increase of inflow. It was concluded that high carbon dioxide exerts a differential effect upon various parts of the pulmonary vascular bed. The authors consider that recognition of regional vasodilatation must qualify any generalization which might be arrived at simply from consideration of inflow or outflow of blood or of alterations in pulmonary arterial pressure alone that high carbon dioxide causes a pulmonary vasoconstriction.

The effects of local alteration in carbon dioxide on the intestinal blood flow has been investigated by Mohamed and Bean (*803*) 1951 by perfusing the dog intestine either completely isolated, or isolated in situ with heparinized dog blood previously equilibrated with gas mixtures of various carbon dioxide content from 0 to 15 percent. Hypercapnemia invariably increased the intestinal blood outflow and inflow, quite independently of any alterations in tone or motility, due to a direct vasodilating action of carbon dioxide on the intestinal blood vessels. There was commonly a predominant inhibition of motility and a diminished intestinal tone which was usually preceded by a transient initial augmentation of motility and tone, occasionally followed by late sporadic tonic contractions. Local hypocapnemia caused a vasoconstriction and decreased intestinal blood flow. Intrapulmonary administration of high carbon dioxide in respiratory gas mixtures caused vasoconstriction of central origin in the intestine isolated in situ except for its extrinsic nerve supply and perfused with normal heparinized blood. The high threshold and relatively low magnitude of this reflex vasoconstriction suggested to the authors that in the intact animal this central nervous regulation of intestinal vessels is not operative except under severe conditions.

For further studies on the action of carbon dioxide on the circulation, papers by the following may be consulted: Binet and Burstein (*785*) 1947; Campbell (*786*) 1950; Holmes, Parry, Draper, and Whitehead (*795*) 1950; Hood (*796*) 1947; and Jourdan, Collet, and Paulon (*797*) 1951.

781. Alella, A. and E. Meda. Modificationi nell'unano della pressione arteriosa e del volume minuto con respirazione di CO_2 a varie concentrazioni. *Boll. Soc. ital. Biol. sper.*, 1948, *24:* 491–492. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 775. Abstr.

782. Altschule, M. D. and W. M. Sulzbach. Tolerance of the human heart to acidosis; reversible changes in RS–T interval during severe acidosis caused by administration of carbon dioxide. *Amer. Heart J.*, 1947, *33:* 458–463. [P]

783. Asmussen, E. CO_2-breathing and output of the heart. *Acta physiol. scand.*, 1943, *6:* 176–186. [P]

784. Bean, J. W., W. P. Mayo, F. O'Donnell, and G. W. Gray. Vascular response in dog lung induced by alterations in pulmonary arterial carbon dioxide tension and by acetylcholine. *Amer. J. Physiol.*, 1951, *166:* 723–732. [P]

785. Binet, L. and M. Burstein. Action du CO_2 sur le tonus des vaisseaux périphériques. *C. R. Soc. Biol., Paris,* 1947, *141:* 488–490. [P]

786. Campbell, G. S. Effect of 10% carbon dioxide on the cardiac response to electrical stimulation of the vagus nerve. *XVIII Intern. physiol. Congr.*, 1950, 142–143.

787. Christensen, B. On the electrocardiographic changes in normal man brought about by changing the carbon dioxide tension in the arterial blood. *Acta med. scand.*, (*Suppl.*), 1946, *206:* 20–28.

788. Durant, T., J. Long, and M. J. Oppenheimer. The effect of carbon dioxide on the initial ventricular deflection of the EKG. *Amer. J. med. Sci.*, 1947, *213:* 633–634. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 362. Abstr.

789. Durant, T., J. Long, M. J. Oppenheimer, and M. R. Wester. Effect of carbon dioxide and other gases on electrocardiogram of the right ventricle. *Proc. Soc. exp. Biol., N. Y.*, 1947, *66:* 479–481. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 348. Abstr.

790. Gibbs, F. A., H. P. Maxwell, and E. L. Gibbs. Volume flow of blood through the brain of man at rest, during hyperventilation and while breathing high CO_2. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 33.

791. Gibbs, F. A., H. Maxwell, and E. L. Gibbs. Volume flow of blood through the human brain. *Arch. Neurol. Psychiat., Chicago*, 1947, *57:* 137–144. [P]

792. Duke, H. N. The action of carbon dioxide on isolated perfused dog lungs. *Quart. J. exp. Physiol.*, 1949, *35:* 25–37. [P]

793. Durant, T., J. Long, and M. J. Oppenheimer. The effect of carbon dioxide on the initial ventricular deflection of the EKG. *Amer. J. med. Sci.*, 1947, *213:* 633–634. [P]

794. Hebb, C. O. and R. H. Nimmo-Smith. Pulmonary vasoconstriction in response to inhalation of carbon dioxide in the isolated perfused lungs of Macacus Rhesus. *Quart. J. exp. Physiol.*, 1948, *34:* 159–163. [P]

795. Holmes, J. H., T. M. Parry, W. B. Draper, and R. W. Whitehead. Plasma volume changes produced by inhalation of carbon dioxide. *J. clin. Invest.*, 1950, *29:* 823. Abstr.

796. Hood, B. Diodrastclearance under kolsyreinhalation. [Diodrast clearance under carbon dioxide inhalation.] *Nord. Med., Stockholm,* 1947, *33:* 34–35.

797. Jourdan, F., A. Collet, and Y. Paulon. Sur la puissance et l'étendue de l'action vasculaire locale de l'anhydride carbonique. *C. R. Soc. Biol., Paris,* 1951, *145:* 732–734. [P]

798. Little, W. J., J. W. Avera, and S. W. Hoebler. Effects of breathing CO_2 on blood pressure and renal circulation in normotensive and hypertensive subjects. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 98–99. [P]

799. Lyman, C. P. Effect of increased carbon dioxide on respiration and heart rate of hibernating hamsters and ground squirrels. *Amer. J. Physiol.*, 1951, *167:* 638–643. [P]

800. Mayerson, S. The use of carbon dioxide in preventing post-exercise orthostatic circulatory insufficiency. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 72.

801. Meeter, E. The effect of carbon dioxide breathing on the metabolism in the isolated heart-lung preparation. *Acta brev. neerl. Physiol.*, 1948, *16:* 31–32. [P]

802. Meeter, E. De invloed van CO_2 in de ademhalingslucht op de stofwisseling van het geisoleerde hart-longpraeparaat. [Influence of CO_2 in inspired air on the metabolism of isolated heart-lung preparation.] *Ned. Tijdschr. Genesk.*, 1948, *92:* 3032–3034.

803. Mohamed, M. S. and J. W. Bean. Local and general alterations of blood carbon dioxide and influence of intestinal motility in regulation of intestinal blood flow. *Amer. J. Physiol.*, 1951, *167:* 413–425. [P]

804. Nisell, O. Effects of oxygen and carbon dioxide on the circulation of isolated and perfused lungs of the cat. *Acta physiol., scand.*, 1948, *16:* 121–127.

805. Patterson, J. L., Jr., E. J. Waits, and M. V. McPhaul. Studies on differential circulatory effects of carbon dioxide. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 102.

806. Penneys, R. A method of administering carbon dioxide at a constant degree of induced anoxemia and its cardiovascular effects. *Johns Hopk. Hosp. Bull.*, 1950, *86:* 107–118.

807. Spencer, J. N., T. M. Parry, R. W. Whitehead, and W. B. Draper. The tolerance of the dog under thiopental sodium anesthesia to high concentrations of carbon dioxide. *J. Pharmacol.*, 1950, *98:* 365–371. [P]

808. Van Euler, U. S. and G. Liljestrand. Effects of inhalation of gas mixtures of varying oxygen and carbon dioxide content. pp. 309–312 in: Observations on the pulmonary arterial blood pressure in the cat. *Acta physiol. scand.*, 1946, *12:* 301–320. [P]

D. BLOOD

The effects of increased carbon dioxide concentrations upon the electrolytes in the blood and tissues have been investigated by Malorny (*809* and *810*) 1948. On the basis of animal experiments, the author finds that all the ion systems used to maintain the balance between acids and bases are affected by increased carbon dioxide. There is a considerable increase of serum calcium and a small diminution of ionized calcium with a resulting increase in the potassium-calcium quotient. Malorny found that this rise was particularly high with lower carbon dioxide tensions of 15 to 53 mm. Hg, whereas it was practically absent with higher tensions of more than 80 mm. Hg. The process of exchange of anions in the blood corpuscle-plasma system was compared with the process of exchange of cations which occurs in the muscle cell-body fluid system and liver cell-body fluid systems. This shifting of ions also has a regulatory effect upon the metabolism of acids and bases. In order to increase the buffering capacity, the muscle cells take up the potassium and sodium ions, whereas, in proportion to its higher buffering power, the hepatic tissue releases these bases, even though not to a fully equivalent extent. The taking up of bases by the muscles at lower carbon dioxide tensions must be understood, according to the author, as a successful regulatory mechanism against acidification of the tissues. By this means the total alkali content of the muscles is increased by about 10 percent. At high carbon dioxide tensions this regulatory mechanism fails. The antagonistic effects of lower and higher carbon dioxide concentrations is also shown in the behavior of the alkali reserve in the blood. If small quantities of carbon dioxide are present in the respired air, the alkali reserve of the animals is at first distinctly raised, dropping subsequently if the carbon dioxide tension is increased.

809. Malorny, G. Das Verhalten der Elektrolyte im Blut und Gewebe bei erhöhten CO_2—Spannungen der Atmungsluft. *Arch. exp. Path. Pharmak.*, 1948, *205:* 667–683. [P]

810. Malorny, G. Mineral shifting between blood and tissue under the influence of increased CO_2 concentrations. Germany. U. S. Zone. Office of naval advisor. pp. C: I–1—C: I–60 in: *Monograph on submarine medicine, Folio IV*, 1948. [P]

E. CEREBROSPINAL FLUID

Spencer, Goldensohn, Whitehead, Grover, and Draper (*812*) 1949 have investigated the pressure responses of the cerebrospinal fluid to diffusion respiration and carbon dioxide inhalation in dogs under light thiopental sodium anesthesia. With diffusion respiration and various concentration of carbon dioxide, the cerebrospinal fluid pressure was seen to rise consistently to at least twice the control value and to an average of 3½ times the control value. During inhalation of 40 percent carbon dioxide in oxygen, the maximum rise in cerebrospinal fluid pressure was usually reached within 5 minutes and amounted to 4½ times the control pressure. Goldensohn, Whitehead, Parry, Spencer, Grover, and Draper (*811*) 1951 pointed out that the rise in mean cerebrospinal fluid pressure could not be correlated directly with changes in systemic arterial pressure or systemic venous pressure. They concluded that the rise in mean cerebrospinal fluid pressure produced by inhalation of high carbon dioxide concentrations is not dependent upon associated changes in the rate and force of respiratory movements.

811. Goldensohn, E. S., R. W. Whitehead, T. M. Parry, J. N. Spencer, R. F. Grover, and W. B. Draper. Studies on diffusion respiration. IX. Effect of diffusion respiration and high concentrations of CO_2 on cerebrospinal fluid pressure of anesthetized dogs. *Amer. J. Physiol.*, 1951, *165:* 334–340. [P]

812. Spencer, J. N., E. S. Goldensohn, R. W. Whitehead, R. F. Grover, and W. B. Draper. Pressure responses of the cerebrospinal fluid to diffusion respiration and carbon dioxide inhalation. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 149. [P]

F. RESPIRATION

Dripps and Comroe (*822*) 1947 and Comroe and Dripps (*818*) 1948 have investigated the respiratory and circulatory responses of normal young men to inhalations of 7.6 and 10.4 percent of carbon dioxide mixtures. When 7.6 percent carbon dioxide in oxygen was inhaled, the average minute volume of respiration was increased to a maximum of 51.5 liters per minute (range, 24 to 102 liters per minute). The pulse rate was increased by 16.7 beats per minute and the blood pressure rose 30.8 mm. Hg systolic and 22.2 mm. Hg diastolic. When 10.4 percent carbon dioxide in oxygen was inhaled, the average maximal minute volume of respiration rose to 76.3 liters per minute (range, 40 to 130 liters per minute). The pulse rate increased 15.6 beats per minute, and the arterial blood pressure rose 33.4 mm. Hg systolic and 25.0 mm. Hg diastolic. In these acute studies when the carbon dioxide inhalation was stopped, respiration and systolic blood pressure returned slowly to normal. The diastolic blood pressure fell abruptly upon removal of the mask and was often lower than the control figures. Comparing the maximal ventilation produced by (1) inhalation of 7.6 percent of carbon dioxide, (2) exhaustive muscular exercise, and (3) maximal voluntary hyperventilation, the authors found that the average ventilation volume for voluntary hyperventilation was 166 liters per minute; that for exhaustive muscular exercise was 110 liters per minute, while the response to high concentrations of carbon dioxide was least.

Holman and Shires (*833*) 1949 carried out quantitative studies of ventilation during inhalation of carbon dioxide in normal and emphysematous patients. These subjects were exposed to 30 percent oxygen and 70 percent nitrogen mixture, and then to a mixture containing 67 percent nitrogen, 30 percent oxygen, and 3 percent carbon dioxide. The subjects were in supine position and at rest. Both the normal subjects and the emphysematous patients showed a considerably variable increase in the minute volume of respiration.

The effect of passive hyperventilation in human subjects for a 24-hour period upon the response to carbon dioxide inhalation has been investigated by Brown, Hemingway, and Visscher (*816*) 1950. Human subjects breathed 3 percent, 5 percent, or 7 percent carbon dioxide in oxygen before and after 24 hours of passively imposed hyperventilation. Plotting the minute volume of respiration against the arterial blood carbon dioxide tension, it was found that the slope of the curve was increased and displaced to the left after hyperventilation. The graph of minute volume as a function of arterial blood pH shows a similar displacement in one subject. The increase in response to carbon dioxide shown to exist after 24 hours of passively imposed hyperventilation cannot be explained entirely on the basis of reduced bicarbonate concentration of the blood which takes place with prolonged overbreathing. For a further report on the effect of hyperventilation on the response to inhalation of carbon dioxide, a paper by Brown, Campbell, Johnson, Hemingway, and Visscher (*815*) 1948 may be consulted. That the respiratory responses to carbon dioxide are not altered by altitude hypoxia is indicated in a report by Weatherby and Burt (*847*) 1944. For a discussion of individual variations in respiratory response to carbon dioxide at altitude, this report should be consulted.

Effects of breathing high carbon dioxide concentrations on animals are reported by the following: Chapin and Rahn (*817*) 1948; Eichenberger (*824*) 1950; Hatsuzo (*831*) 1951; Miller, Brown, and Varco (*836*) 1950; Sass-Kortsak, Peyser, and Versar (*841*) 1947; Schaefer, Cornish, and Smith (*842*) 1951; and Valeriok and De Carli (*845*) 1950. These acute studies generally indicate an increase in respiratory activity from breathing high carbon dioxide mixtures. In the study by Miller, Brown, and Varco (*836*) 1950, it was found that respiratory depression occurred in dogs breathing mixtures containing carbon dioxide in concentrations greater than 15 percent. In rabbits, Eichenberger (*824*) 1950 distinguished between an activating influence of carbon dioxide (with concentrations up to 7.5 percent) and an inhibitory action on respiration (with concentrations above 7.5 percent carbon dioxide). Valeriod and De Carli (*845*) 1950 found that breathing air containing 6 percent carbon dioxide increased the depth and frequency of respiration of guinea pigs when in a horizontal position, but with animals in an orthostatic position there was only an increase in depth. These reactions disappeared entirely when animals were refrigerated below 23° C. In view of the very slight ventilatory response to carbon dioxide of diving mammals as compared to nondiving mammals, Chapin and Rahn (*817*) 1948 investigated the effect of inhalation of high carbon dioxide mixtures upon the ventilation of the unanesthetized beaver. The minute ventilation during the control period was compared with the 6th to 10th minute after breathing the various carbon dioxide mixtures. With 3.8 percent carbon dioxide in air, there was a 27 percent increase in ventilation. With 6.5 percent carbon dioxide in air, the increase in ventilation was 84

percent. With 11.4 percent carbon dioxide in air, the increase was 252 percent. These values are somewhat lower than those obtained on unanesthetized dogs in the author's laboratory and differed considerably from those obtained on human subjects. For studies of the action of carbon dioxide on central nervous respiratory mechanisms, papers by the following may be consulted: Gellhorn (*826*) 1943; Gollwitzer-Meier and Pinotti (*827*) 1947; Heymans, Bouckaert, and Dautrebande (*832*) 1950; Leusen (*834*) 1950; Gollwitzer-Meier (*828, 829*) 1950; Gray (*830*) 1945; Santenoise, Grandpierre, Biget, Cotlenko, Lemaire, and Ramanamanjary (*840*) 1950; and Wang and Nims (*846*) 1948.

The effects of carbon dioxide on pulmonary circulation have been discussed in a previous section (IV–C, heart and circulation (p. 59)). For further reports upon this subject, papers by the following are included: Bean and Mayo (*814*) 1951, Dirken and Heemstra (*821*) 1947–48, Duke (*823*) 1949, and Nisell (*837*) 1950.

Meessen (*835*) 1948 exposed rats, guinea pigs, rabbits, and dogs to mixtures of carbon dioxide in air in which the carbon dioxide concentrations ranged from 1 to 26 percent while the oxygen pressure remained normal. These mixtures were inhaled for periods ranging from 5 to 6 weeks. The animals exhibited degenerative changes in the lungs, liver, kidney, and brain believed to be the result of increased carbon dioxide tension and not caused by anoxemia. The pulmonary reactions were similar to those elicited by experimental oxygen poisoning and by poisoning with phosgene.

For further references on the effects of carbon dioxide on respiration, reference may be made to papers by the following: Beadle and Beadle (*813*) 1949; Cordier and Cordier (*819*) 1950; Craig, Stubbs, and Marzulli (*820*) 1948; Fleisch and Lehner (*825*) 1949; Nisell (*838*) 1951; Pinotti (*839*) 1946; Shires and Eyer (*843*) 1950; and Travia and Cordone (*844*) 1946.

813. Beadle, L. C. and S. F. Beadle. Carbon dioxide narcosis. *Nature, Lond.*, 1949, *164:* 235.

814. Bean, J. W. and W. P. Mayo. Influence of alterations in pulmonary arterial CO_2 on pulmonary volume and blood flow. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 11.

815. Brown, E. B., Jr., G. S. Campbell, M. N. Johnson, A. Hemingway, and M. B. Visscher. Changes in response to inhalation of CO_2 before and after 24 hours of hyperventilation in man. *J. appl. Physiol.*, 1948, *1:* 333–338. [P]

816. Brown, E. B., Jr., A. Hemingway, and M. B. Visscher. Arterial blood pH and pCO_2 changes in response to CO_2 inhalation after 24 hours of passive hyperventilation. *J. appl. Physiol.*, 1950, *2:* 544–548.

817. Chapin, L. L. and H. Rahn. The effect of CO_2 upon the ventilation response of the beaver. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 19–20.

818. Comroe, T. H., Jr. and R. D. Dripps. The hyperpnea produced in normal man by maximal voluntary hyperventilation, by inhalation of carbon dioxide and by severe muscular exercise. *Amer. J. med. Sci.*, 1947, *213:* 246–247. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 141. Abstr.

819. Cordier, J. and G. Cordier. Modifications du pH, de l'acide carbonique total et du sucre libre de l'humeur aqueuse au cours de l'acidose gazeuse. *C. R. Soc. Biol., Paris,* 1949, *143:* 432–433. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 797.

820. Craig, F. N., J. Stubbs, and F. N. Marzulli. Analysis of combined effects of exercise and carbon dioxide inhalation on pulmonary ventilation in man. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 24. [P]

821. Dirken, M. N. J. and H. Heemstra. Agents acting on the lung circulation. *Quart. J. exp. Physiol.*, 1947–48, *34:* 227–241. [P]

822. Dripps, R. D. and J. H. Comroe, Jr. The respiratory and circulatory response of normal man to inhalation of 7.6 and 10.4 per cent CO_2 with a comparison of the maximal ventilation produced by severe muscular exercise, inhalation of CO_2 and maximal voluntary hyperventilation. *Amer. J. Physiol.*, 1947, *149:* 43–51. *Med. J. Aust.*, 1947, *2:* 432. Abstr. [P]

823. Duke, H. The effect of carbon dioxide on perfused lungs. *J. Physiol.*, 1949, *108:* 59P. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 465.

824. Eichenberger, E. Über die Wirkung der Kohlensäure auf die Atmung des Kaninchens. *Helvet. physiol. pharm. Acta,* 1949, *7:* 55–74. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 462.

825. Fleisch, A. and F. Lehner. Die respiratorische Mittellage. *Helvet. physiol. pharm. Acta,* 1949, *7:* 410–426. [P]

826. Gellhorn, E. Adjustment reactions to carbon dioxide. pp. 21–36 in: *Autonomic regulations. Their significance for physiology, psychology, and neuropsychiatry.* New York, Interscience Publishers, Inc., 1943, 308 pp.

827. Gollwitzer-Meier, K. and O. Pinotti. Über die Nachdauer (Hysteresis) der Erregung des Atemzentrums bei der Kohlensäureatmung. *Pflüg. Arch. ges. Physiol.*, 1947, *249:* 3–16. [P]

828. Gollwitzer-Meier, K. Über das Atemvolumen bei gleichzeitiger Einwirkung von Kohlensäureüberschuss und Sauerstoffmangel. *Bull. fac. Méd.*, 1949, *12:* 166–174. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1495.

829. Gollwitzer-Meier, K. Über das Atemvolumen bei der gleichzeitigen Einwirkung von Kohlensäureüberschuss und Sauerstoffmangel. *Pflüg. Arch. ges. Physiol.*, 1949, *251:* 335–343. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 604.

830. Gray, J. S. The multiple factor theory of respiratory regulation: The isolation and quantification of the independent effects of H ion, CO_2, and O_2 on respiratory ventilation. U. S. AAF. Randolph Field, Texas. School of aviation medicine. *Project 386, Rept. no. 1*, 7 May 1945, 22 pp. [M]

831. Hatsuzo, K. Studies on normal respiration of frog. Part I. Normal breathing and carbon dioxide effect on it.

Nihon Seiri. Z., 1951, *13:* (Japanese text pagination), 319–322. (English text pagination), 322. (In Japanese with English summary.)

832. Heymans, C., J. J. Bouckaert, and L. Dautrebande. Importance comparative de l'action centrale directe et de l'influence réflexe du CO_2 sur la respiration. *Experientia*, 1950, *6:* 390. [P]

833. Holman, J. and G. T. Shires. Quantitative studies of ventilation during inhalation of carbon dioxide in normal and emphysematous patients. *Amer. Heart J.*, 1949, *37:* 1101–1109. [P]

834. Leusen, I. Concerning the specificity of the carbon dioxide action on the respiratory center. *XVIII Intern. physiol. Congr.*, 1950, 336–337. *Arch. int. Physiol.*, 1950, *57:* 456–458. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 541. Abstr. [P]

835. Meessen, H. Chronic carbon dioxide poisoning. *Arch. Path., Chicago*, 1948, *45:* 36–40. [P]

836. Miller, F. A., E. B. Brown, and R. L. Varco. Certain effects in dogs of inspiring 15–30% carbon dioxide. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 89.

837. Nisell, O. I. The action of oxygen and carbon dioxide on the bronchioles and vessels of the isolated perfused lungs. *Acta physiol. scand.* (*Suppl.*), 1950, *73:* 7–59. [P]

838. Nisell, O. The influence of carbon dioxide on the respiratory movements of isolated perfused lungs. *Acta physiol. scand.*, 1951, *23:* 352–360.

839. Pinotti, O. Influenza della tensione del CO_2 del sangue sulla eccitabilita riflessa del centro vasocostrittore. *Boll. Soc. ital. Biol. sper.*, 1946, *22:* 87–89.

840. Santenoise, D., R. Grandpierre, P. Biget, V. Cotlenko, R. Lemaire, and W. Ramanamanjary. Influence de l'inhalation de doses progressivement croissantes de CO_2 sur l'ampliation thoracique. *J. Physiol., Paris*, 1950, *42:* 721–724. [P]

841. Sass-Kortsak, A., E. Peyser, and F. Versar. Sauerstoff und Kohlensäure der Einatmungsluft als Regulator des Lungenvolumens. *Helvet. physiol. pharm. acta.*, 1947, *5:* C46–C47. [P]

842. Schaefer, K. E., E. R. Cornish, and F. S. Smith. Oxygen consumption and carbon dioxide excretion of guinea pigs under basal conditions on air and exposed for four hours to 3% carbon dioxide and 21% oxygen. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 015.03.04*, June 1951, 8 pp.

843. Shires, G. T. and S. W. Eyer. Studies in diffusion respiration. U. S. Navy. NMRI. *Project NM 001 056.03.01*, 14 June, 1950. *J. Aviat. Med.*, 1951, *22:* 22–30. [P]

844. Travia, L. and M. Cordone. L'anidrasi carbonica nel meccanismo respiratorio ed azione del CO_2 sull'attività respiratoria dell'emoglobina. *Riv. Med. aero., Roma*, 1946, *9:* 111–120. (English, French, Spanish, and German summaries.) [P]

845. Valerio, J. and F. De Carli. Azione dell'anidride carbonica sul reflesso respiratorio ortostatico nelle cavie a temperature corporea normale e con raffreddamento graduale. *Boll. Soc. ital. Biol. sper.*, 1950, *26:* 929–930. [P]

846. Wang, S. C. and L. F. Nims. The effect of various anesthetics and decerebration on the CO_2 stimulating action on respiration in cats. *J. Pharmacol.*, 1948, *92:* 187–195.

847. Weatherby, J. H. and A. S. Burt. Individual variation in respiratory response to carbon dioxide at altitude. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project X–402* (*Av–216–f*), *Rept. no. 1*, 25 July 1944, 5 pp.

G. ALIMENTARY TRACT

Breathing high carbon dioxide mixtures by dogs was found in experiments of Stickney, Northup, and Van Liere (*850*) 1948 to delay the gastric emptying time proportionally to the concentration of carbon dioxide in the inspired air. When the carbon dioxide range was between 6 and 8 percent, there was an average increase in gastric emptying time from 15 to over 100 percent. Between 8 and 10 percent carbon dioxide caused an increase of 67 to over 288 percent. Carbon dioxide concentrations between 10 and 12 percent produced an increase in gastric emptying time between 73 and over 300 percent. Northup, Stickney, and Van Liere (*849*) 1949 also found that high carbon dioxide mixtures in dogs and rats depressed the motility of the intestines. In the dogs, intestinal motility was depressed by a concentration of carbon dioxide of 7.5 percent or more and in the rats by a concentration of 15 percent or more. According to Cordier and Chanel (*848*) 1950, high carbon dioxide mixtures in the rat retard intestinal absorption of glucose. Exposure to hypoxia (5 percent oxygen) was found to reinforce the retarding effect of carbon dioxide on intestinal absorption of glucose in the rat. The narcotic effect of carbon dioxide was also augmented by hypoxemia.

848. Cordier, D. and J. Chanel. Influence de la tension d'anhydride carbonique dans l'air inspiré sur la vitesse de l'absorption intestinale des solutions isotoniques de glucose chez le rat anoxique. *J. Physiol., Paris*, 1950, *42:* 574–576. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 760. [P]

849. Northup, D. W., J. C. Stickney, and E. J. Van Liere. Effect of carbon dioxide on intestinal motility. *Amer. J. Physiol.*, 1949, *158:* 119–121. [P]

850. Stickney, J. C., D. W. Northup, and E. J. Van Liere. Effect of increased carbon dioxide in inspired air on gastric emptying in dogs. *Amer. J. Physiol.*, 1948, *155:* 471. Abstr.

H. METABOLISM

For a comprehensive report on metabolism and other effects of increased carbon dioxide concentrations in the inhaled air, a report by Schaefer (*860*) 1948 should be consulted. The author points out that prolonged exposure to 3 percent carbon dioxide in human subjects results in a distinct decrease of the excitability of the respiratory center after 3 days. With physical exertion during prolonged exposure to carbon dioxide, an improved oxygen intake and carbon dioxide release is found as compared with the same exertion during a short

exposure to carbon dioxide. Under the influence of carbon dioxide, the acid-base balance is maintained at first by emergency measures such as an increased pulmonary ventilation, retention of bases by the kidneys, an increased ammonia excretion, and sometimes by increased hydrochloric acid production of the stomach. After approximately 3 days in a carbon dioxide atmosphere of 3 percent, the buffer system of the blood is adapted by increase of the alkaline reserve to such an extent that it is able to keep the blood pH constant without the emergency measures. The author draws attention to a drop of pulse rate as exposure to carbon dioxide continues. The potassium-calcium quotient rises in several test subjects during the adaptation to carbon dioxide. At first there is a sympathicotonic phase which is followed by a vagotonia in the course of adaptation to carbon dioxide. The central nervous system shows a diminished efficiency and there is no evidence of adaptation here. There is a reduced chronaxie with simultaneous drop of the rheobase during the first day of exposure, while the chronaxie was prolonged to twice its basal value and the rheobase increased concurrently with prolonged action of carbon dioxide.

In experiments reported by Endo (*853*) 1944, dogs were kept in an atmosphere containing 10 to 14 percent carbon dioxide and the hemoglobin, protein, colloid osmotic pressure, sugar, lactic acid, carbon dioxide, and sodium chloride determined in the blood both entering and leaving the gastrocnemius muscle while at rest and during work. During work in an atmosphere rich in carbon dioxide, the carbon dioxide in the blood leaving the muscle was higher than when ordinary air was breathed. The protein was increased in the outgoing blood, but the colloid osmotic pressure was decreased. This suggested that the protein is largely in the form of globulin. In a high carbon dioxide atmosphere there was found to be a smaller sugar utilization and lactic acid formation than with ordinary air. The formation of carbon dioxide in the muscle was also decreased and the oxygen debt increased. The blood circulating time was only slightly increased by high concentrations of carbon dioxide, but muscle fatigue was found to occur sooner.

In normal anesthetized cats breathing 34 percent carbon dioxide in oxygen, Mackay (*856*) 1947 found a rapid rise in plasma potassium reaching a peak in 5½ minutes, then gradually returning to about normal in approximately 30 minutes, while high carbon dioxide respiration was being continued. Adrenalectomized cats breathing high carbon dioxide showed a similar but smaller rise. These findings suggest to the author the possible participation of adrenalhepatic mechanisms in the carbon dioxide effect, but they indicate definitely that some other mechanism must also be involved. Cats eviscerated prior to administration of carbon dioxide showed a small rise in plasma potassium, probably released from the muscles to maintain the acid-base balance. In all of the cats high carbon dioxide levels resulted in initial stimulation of respiration followed by a sudden depression as the carbon dioxide passed from the excitatory to the narcotic level. The height of stimulation and depth of depression usually occurred within about five minutes on carbon dioxide. Neither the adrenalectomized or eviscerated cats showed such a remarkable increase in respiration, as measured by minute volume after depression, although the adrenalectomized cats did exhibit a very large increase in tidal volume.

The literature does not contain reports of investigation of metabolic changes following prolonged exposure in human subjects to carbon dioxide. However, Pointner (*858*) 1948 described a decrease in alkaline reserve in dogs given gas mixtures containing carbon dioxide from 12 to 20 percent in short experiments. Six human test subjects remained for 4 days with concentrations of 2.5 to 3 percent. Dogs remained for 10 days to 3 weeks under percentages of 3 to 6 of carbon dioxide. In all cases, an increase of the carbon dioxide absorption curve could be observed. This increase of alkaline reserve did not occur when heavy work was done. Human subjects and dogs were given the short stress of a higher percentage of carbon dioxide (up to 20 percent for the human subjects and 30 percent for the animals). While the alkaline reserve of the test subjects showed a considerable decrease, there was hardly any change in the case of the dogs which had become more readily adapted to prolonged inhalation of carbon dioxide than did human subjects. The author recommended that a potassium buffer salt be given to crew members during critical atmospheric conditions. In animal studies conducted by Schaefer, Storr, and Scheer (*861*) 1948, guinea pigs were kept under various carbon dioxide concentrations from 3 to 24 percent. Two animals were sacrificed within the first 3 days to determine the alkaline reserve and to get a whole blood count. Tissue was taken from the kidneys and liver to measure oxygen consumption. There was effective adaptation within 11 to 13 days. In all animals, the body weight was diminished in the early part of the tests, and weight loss was greater with 3 percent carbon dioxide than with higher concentrations. Within several days the weight became stabilized. With 3 percent carbon dioxide inhalation, the stable

weight level was below the basal value. With higher concentrations, it again reached the preexposure level. For a concentration of 3 percent carbon dioxide and less, the amount of hyperventilation was adequate to prevent accumulation of carbon dioxide. An accumulation of carbon dioxide did appear during the first days and with a further increase of carbon dioxide. This was overcome following the onset of a gradual increase of the alkaline reserve. After an initial, moderate drop in alkaline reserve, it became increased and the extent of this increase depended upon the concentration of the inhaled carbon dioxide. After transfer to normal air, the alkaline reserve dropped to the initial value. The blood sugar was found to be elevated during exposure to 3 percent and 12 percent carbon dioxide in the first days and subsequently dropped below the basal values. During the initial phase of excitation, there was an increase in nonprotein nitrogen, while the beginning of the second phase, the nonprotein nitrogen in the urine decreased. Hence, during the first phase, the organism is not considered accommodated to the carbon dioxide effect. In the second phase, the threshold for excitation of the central nervous system is raised to a higher level as contrasted to a lower level in the first phase.

In an investigation of gas exchange in human subjects in submarines with carbon dioxide concentrations at approximately 3.4 percent, Schaefer (*859*) 1948 reported a diminution of oxygen consumption and an increase in the release of carbon dioxide with an increased respiratory quotient. Haebisch (*854*) 1948, in reporting studies on crew members in submarines, draws attention to a respiratory quotient of one and a diminution of oxygen absorption.

Studies of Bain and Klein (*851*) 1949 reveal a lowering of lactate and pyruvate levels in the brains of normal cats following respiration in 10 to 30 percent carbon dioxide mixtures. Brain tissue was analyzed after freezing with liquid air. In these animals there was little change in the glucose or phosphate concentrations. In convulsed animals there was considerable limitation of the expected rise in lactate, pyruvate, and inorganic phosphate. There was a rise in brain glucose level but little effect on the brain plasma-glucose ratios. Colldah (*852*) 1949 has reported studies on tissue respiration, especially in the liver of animals exposed to high carbon dioxide concentrations before sacrifice. Inhalation of carbon dioxide in narcotic concentration (20 to 25 percent) lowered tissue respiration in the liver, even if oxygen deficiency had been avoided. Tissue respiration in the liver was normal with lower carbon dioxide concentrations without the narcotizing effect or reduction of the frequency of respiration. With narcotizing concentrations of carbon dioxide there was a great increase of inorganic phosphorus in the blood.

For further studies of the effect of carbon dioxide on metabolic function, papers by Kuroda (*855*) 1948 and Mason (*957*) 1947 may be referred to.

851. Bain, J. A. and J. R. Klein. Effect of carbon dioxide on brain glucose, lactate, pyruvate, and phosphates. *Amer. J. Physiol.*, 1949, *158:* 478–484. [P]

852. Colldah, H. On the changes in the organism resulting from insufficient gas exchange. III. On the cause of the lowered tissue respiration in insufficient gas exchange and on the effect of high carbon dioxide concentrations on tissue respiration. *Acta med. scand.*, 1949, *132:* 378–383. [P]

853. Endo, K. Über die Veränderungen der Stoffumsatze des Muskels in der Ruhe und bei der Arbeit unter CO_2 Atmung. *Tôhoku J. exp. Med.*, 1944, *47:* 223–235. (German text.) (English pagination.) [P]

854. Haebisch, H. The gases contained in the air of submarines and gas metabolism during rest in the submarine environment. pp. C:III–1—C:III–17 in: *Monograph on submarine medicine, Folio IV*, Germany. U. S. Zone. Office of naval advisor. 1948.

855. Kuroda, M. [The effect of inhalation of CO_2 for a long period of time upon the body, especially on the action of urinary function.] *Jap. J. Hyg.*, 1948, *2:* 21–25. (English pagination.) [P]

856. Mackay, J. L. Effects of a narcotic level of carbon dioxide on the plasma potassium and respiration of cats. *Amer. J. Physiol.*, 1947, *151:* 469–478. [P]

857. Mason, E. C. The action of carbon dioxide in water mobilization. *Ann. intern. Med.*, 1947, *26:* 561–568. [P]

858. Pointner, R. Carbon dioxide absorption curve and the mineral metabolism in an atmosphere containing carbon dioxide and the influence effective on both of them. pp. C:II–1—C:II–24 in: *Monograph on submarine medicine, Folio IV*, Germany. U. S. Zone. Office of naval advisor. 1948.

859. Schaefer, K. E. The content of oxygen and carbon dioxide in the submarine air. pp. B: I–29—B: I–30 in: *Monograph on submarine medicine, Folio I*, Germany. U. S. Zone, Office of naval advisor. 1948.

860. Schaefer, K. E. The regulation of the blood circulation of man on submarines. The adaptation to increased CO_2 concentrations in the inhaled air. pp. C: 1–61 in: *Monograph on submarine medicine, Folio 5*, Germany. U. S. Zone. Office of naval advisor. 1948.

861. Schaefer, K. E., H. Storr, and K. Scheer. Physiological and pathological investigations with guinea pigs exposed to various carbon dioxide concentrations. Part I. Physiological investigations. pp. C IX–1—C IX–18 in: *Monograph on submarine medicine, Folio VI*, Germany. U. S. Zone. Office of naval advisor. 1948. [P]

I. ENDOCRINE GLANDS

Schäfer, Klein, and Zinck (*863*) 1950 found in experiments with dogs that adrenalin injections during acute exposure to 3 percent carbon dioxide produced a strong increase of the blood sugar level. After prolonged exposure to carbon dioxide, adrenalin injection gave only a slight blood sugar rise.

The blood sugar also decreased. Morphologically it was shown that after chronic carbon dioxide exposure, the chromaffin characteristic of the adrenal medullary cells was reduced. Gross vacuolation of the medullary and cortical cells was seen. The zona reticularis was hypertrophied with continuous carbon dioxide exposure. Evidence indicated that the first 17 days of exposure constitute a rising phase of adrenal activity followed by a slow decrease of activity. After prolonged exposure to 3 percent carbon dioxide, the epinephrine content of the adrenal medulla was found to be decreased as measured by the effect of extracts from the glands on the blood pressure of decerebrated cats. That exposure to high carbon dioxide is in itself an alarm reaction-producing stimulus, perhaps through its action on the acid-base balance of the blood, has been concluded by Fortier (*862*) 1949. Exposure of albino rats to an atmosphere containing 15 percent carbon dioxide, 19 percent oxygen, and 66 percent nitrogen for 38 hours resulted in significant hypertrophy of the adrenal cortex together with splenic and thymic involution. The object of this study was to examine whether alkalosis represents a necessary factor to the initiation of the alarm reaction or whether it is to be considered as but one form of nonspecific stress. The results indicated to the author that alkaline shift of the acid-base balance cannot be the necessary prerequisite to the development of the alarm reaction.

862. Fortier, C. Effect of atmospheric carbon dioxide on adrenal cortical hyperplasia and associated changes due to stress. *Proc. Soc. exp. Biol., N. Y.*, 1949, *70:* 76–78.

863. Schäfer, K. E., H. Klein, and K. H. Zinck. Experimentelle Untersuchungen über den Zusammenhang von Mark und Rinde der Nebenniere unter Langdauernder CO_2—Einwirkung. *Klin. Wschr.*, 1950, *28:* 179–184. [P]

J. ACCLIMATIZATION

Schäfer (*869*) 1949 carried out experiments on human subjects involving continuous exposure to 3 percent carbon dioxide and 21 percent oxygen over periods up to 6 days, followed by intermittent 8-hour exposures to 3 percent carbon dioxide and 21 percent oxygen over a period of 192 hours. The depressed state was reached during the first part of the experiment with 6 days of continuous exposure. This state of depression did not change during the second part of the experiment with 8 days of intermittent exposure to carbon dioxide, in spite of relatively long time periods on ordinary air (16 hours a day). A period of 5 days on air was required before the urine suddenly showed a very large output of carbon dioxide and at the same time the pulse rate, blood alkaline reserve, and chronaxie returned to pretest levels. During the continuous and intermittent periods of exposure to carbon dioxide, the pulse rate was lowered, the blood alkaline reserve was increased, and the chronaxie prolonged. The carbon dioxide excretion in the urine was reduced to a minimum during the exposure to carbon dioxide. In 1950, Schafer (*868*) again called attention to a biphasic reaction produced by exposure of men to 3 percent carbon dioxide in air over a period of 6 or more days. This reaction consists of an initial period of excitation followed by depression. Tests of letter canceling and hand steadying, chronaxie measurements and changes in the electroencephalographic pattern confirmed the subjective sensations. Excitability of the respiratory center decreased while the alkaline reserve of the blood increased, mainly due to retention of alkalis by the kidney. Experiments with guinea pigs, rats, mice, and dogs using carbon dioxide concentrations from 3 to 24 percent also revealed biphasic variations. At lower carbon dioxide concentrations around 3 percent, the excitatory phase was not regularly observed. Higher carbon dioxide concentrations of 12 percent or more exhibited both phases distinctly.

According to Otis (*867*) 1949, the principal change in chronic exposure of mice to high carbon dioxide concentrations (up to 20 percent carbon dioxide) is an apparent increase of ventilation and an increase in the alkaline reserve of the blood. Mice subjected to gradually increasing carbon dioxide tensions up to a final tension of 20 percent carbon dioxide had their tolerance increased, but when suddenly exposed to room atmosphere, convulsed and died. If the decrease in carbon dioxide percentage was gradually accomplished, the mice encountered no difficulty. This finding is of significance in view of the cases of collapse of submarine personnel coming out on deck after surfacing following long periods of submergence. In man after 3 days exposure to 3 percent carbon dioxide, there is an increase in blood bicarbonate. With continued exposure the hyperpnea diminishes.

In healthy men working and resting in a chamber for 5 to 8 days in an atmosphere of 2.5 to 3 percent carbon dioxide, Häbisch (*865*) 1949 found that the subjects became adapted to the increased carbon dioxide concentration so long as this carbon dioxide tension was maintained for longer than 3 days. This adaptation could be maintained through intermittent exposure in air with increased carbon dioxide tensions and also the adaptation reaction could be shortened by a continuous carbon dioxide stimulus. Häbisch considered that adaptation to carbon dioxide was on an autonomic-humoral basis.

Adaptation manifested itself in a reduction of ventilation and a rise of alveolar carbon dioxide tension at rest and during exercise. There were marked individual variations in the degree of adaptation.

Karlin and Curtis (*866*) 1945 have reported observations on the efficiency of submarine personnel during prolonged submergence, when the atmospheric oxygen was maintained at 17 percent and the carbon dioxide at 3 percent. The purpose of this investigation was to determine whether the operating efficiency of submarine personnel deteriorated during submergence when the atmospheric oxygen was maintained at 17 percent and the carbon dioxide at 3 percent for extended periods. In these studies the air in the submarine reached 3 percent carbon dioxide after 18 hours of submergence, and this level was held for another 68 hours. The subjects showed a decreased capacity for physical work and a decrement in night visual efficiency in approximately one-third of the ship's company. There was striking reduction in mental efficiency of all hands and a decrease in efficiency of intercommunications. A noticeable, but unproven, decrease in efficiency of radar, and bow and stern plane watches was reported. There was no reliable decrease of efficiency of sonar performance, "Christmas tree" watch, or in remembering numbers.

For further studies on acclimatization, papers by the following may be consulted: Gray (*864*) 1945 and White (*870* and *871*) 1948.

864. Gray, J. S. The multiple factor theory of respiratory regulation. III. Changes in sensitivity to CO_2 in prolonged acapnia and hypercapnia. U. S. AAF. Randolph Field, Texas. School of aviation medicine. *Project 386, Rept. no. 3,* 21 November 1945, 47 pp. [M] [R]

865. Habisch, H. Über den Gaswechsel bei Ruhe und Arbeit unter Kurz-und langfristiger Kohlensäureeinwirkung. *Pflüg. Arch. ges. Physiol.,* 1949, *251:* 594–608. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1210. [P]

866. Karlin, J. E. and J. F. Curtis. Observations on efficiency of submarine personnel during prolonged submergence when the atmospheric oxygen is maintained at 17% and the carbon dioxide at 3%. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–516 (Sub. no. 105), Final rept.,* 27 July 1945, 46 pp.

867. Otis, A. B. Acclimatization to carbon dioxide, carbon monoxide and low oxygen. pp. 23–25. U. S. NRC–CAM. *Conference on acclimatization,* 17 June 1949, 29 pp.

868. Schaefer, K. E. Adaptation of men and animals during prolonged exposure to increased carbon dioxide concentrations. *Amer. J. Physiol.,* 1950, *163:* 747.

869. Schäfer, K. Atmung und Säure-Basengleichgewicht bei langdauerndem Aufenthalt in 3% CO_2. *Pflüg. Arch. ges. Physiol.,* 1949, *251:* 689–715. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1211. [P]

870. White, C. S. Estimated tolerance of human subjects to various carbon dioxide time concentrations. Appendix No. 1. Calculation of carbon dioxide percentage equivalents at sea level and various altitudes. Lovelace clinic. *Project 200, Rept. no. 1,* 12 October 1948.

871. White, C. S. Estimated tolerance of human subjects to various carbon dioxide-time concentrations. Lovelace clinic. *Project 200, Rept. no. 2,* 27 July 1948.

K. PATHOLOGICAL CHANGES

The literature contains a number of studies of pathological changes resulting from experimental exposure to high concentrations of carbon dioxide. In 1947, Meessen (*872*) reported on exposure of rats, cats, and dogs to 4.5 percent carbon dioxide in air for 13 days. In these animals there were irreversible changes including damage of the alveolar walls of the lungs and cell necrosis with dead cells and debris in the liver, kidney, and brain. In 1948, Meessen (*873*) subjected rats and guinea pigs to carbon dioxide concentrations of 1 to 26 percent for periods of 5 hours to 6 weeks. If animals were killed immediately after exposure, a high degree of hyperemia of the lung was found. Pulmonary edema was seen if the animal died in air with high carbon dioxide concentrations. In some cases fluid entirely obstructed the alveoli. On prolonged exposure, the alveoli of the lungs were dilated as in emphysema with dense infiltration of leukocytes in extensive areas. Hyperemia extended throughout the liver. In rats, after 4 days of exposure to 20 percent carbon dioxide, there were extensive, irreversible hepatic changes. In some liver cells the nuclei were pyknotic. After exposure to 14 percent carbon dioxide for 48 hours, the kidneys were hyperemic and nephrotic. In these same animals there were irreversible changes in the central neurons. In guinea pigs exposed to carbon dioxide concentrations of 3, 12, and 24 percent at an equal oxygen tension, Zinck (*875*) 1948 found that with up to 12 percent carbon dioxide there was a shifting of the blood from the splanchnic area towards the heart and lungs. With 24 percent carbon dioxide, the lungs were rather anemic and the abdominal organs showed a greater capillary vascularization. The musculature of the caudal extremities showed constricted capillaries in all experiments. The liver and kidneys appeared to be the first organs impaired, showing changes which disappeared on recovery. In the liver there was reduction of the glycogen accompanied by moderate pericapillary and peripheral deposition of fat with simultaneous lipemia. The straight uriniferous tubules showed vacuolar degeneration and necroses. With high carbon dioxide concentrations, there were fat deposits in renal pyramids. The glomeruli were swollen.

There was a reduction of lipoid substances in the adrenal glands and the medullary cells were coarsely vacuolized, apparently indicating a reduction of epinephrine. There was atelectasis, interstitial pneumonia, hyperplasia of the alveolar epithelium and desquamation in the lungs. Glycogen disappeared from the heart. Sometimes the striations of the heart muscle fibers became indistinct and edema was present. There was edema at the base of the left coronary artery. The spleen was contracted, and with 24 percent carbon dioxide an edema of the reticulum was observed.

In a study of central nervous system changes resulting from increased concentrations of carbon dioxide, Stephens (*874*) 1951 exposed rats to an increase of carbon dioxide percentage to 20 percent within 2 hours and then up to 38 percent and finally to 43.2 percent. As the carbon dioxide percentage rose above 15 percent, the activity of the animals was greatly decreased. In chronic experiments, rats were exposed for periods of 10 to 166 days to carbon dioxide concentrations ranging between 6 and 10 percent and the oxygen between 18 and 23 percent. Cells which are most sensitive to hypoxia (such as those of the cerebral cortex) were found to be protected from severe histopathological changes. The cells of the primitive levels of the brain (less sensitive to oxygen lack) sustained the greatest structural damage as result of high carbon dioxide. The nerve cell damage during carbon dioxide exposure in the prolonged experiments was believed by the author to be due to toxic cellular metabolites rather than hypoxia. The cell changes in animals exposed chronically to concentrations of carbon dioxide rarely exceeding 10 percent were reversible. Also in the acute exposures the cell changes were generally reversible. Irreversible changes were seen in some large motor cells. In the acute experiments, the neurons were slightly swollen and there was chromatolysis, more pronounced at the periphery of the cells. There was swelling of the nucleus and nucleolus, and also marked vacuolation. In the chronic experiments there was severe swelling of the cells with chromatolysis.

In guinea pigs exposed to 3 percent carbon dioxide with adequate oxygen, Klein (*764*) 1949 reported vacuolar degeneration of the cells of the hypophysis. Animals exposed for 12 to 14 days to this concentration of carbon dioxide demonstrated maximum vacuolation in the chromophobe cells. For studies on the pathological changes in the liver following exposure of guinea pigs to 12 percent carbon dioxide, a report by Zinck (*876*) 1949 may be consulted.

872. Meessen, H. Organveränderungen nach experimenteller Kohlendioxydvergiftung. *Schweiz. Med. Wschr.*, 1947, *77:* 1135–1136. [P]

873. Meessen, H. Pathological findings after carbon dioxide intoxication. pp. C X–1—C X–9 in: *Monograph on submarine medicine, Folio VI,* Germany. U. S. Zone. Office of naval advisor. 1948. [P]

874. Stephens, W. M. The central nervous system changes resulting from increased concentrations of carbon dioxide. *J. neuropath. clin. neurol.*, 1951, *1:* 88–97. [P]

875. Zinck, K. H. Physiological and pathological investigations with guinea pigs exposed to various carbon dioxide concentrations. Part II. Pathological investigations. Morphological findings with the carbon dioxide poisoning of guinea pigs compared with the damages of the tissues in cases of hypoxydosis and oxygen poisoning. pp. C IX–1—C IX–40 in: *Monograph on submarine medicine, Folio VI,* Germany. U. S. Zone. Office of naval advisor. 1948. [P]

876. Zinck, K. H. Organveränderungen bei Kohlensäureeinwirkung verschiedener Konzentration und Dauer auf das Meerschweinchen. *Verh. dtsch. path. Ges.*, 1949, *33:* 89–95. [P]

V. HEAT AND HUMIDITY PROBLEMS

A. GENERAL CONSIDERATIONS OF TEMPERATURE, HUMIDITY, AND CLIMATE

One of the foremost habitability problems in submarines arises from excess temperature and humidity. Conditions of insupportable heat and humidity may indeed be responsible for failure of the patrol, and it is reported that German submarines in World War II were forced to abandon patrols and turn back to port because of loss of efficiency of the crews due to heat and humidity. In the later stages of the war it was realized in the German submarine service that adequate air conditioning was essential, and some submarines were so conditioned. In the United States Navy, air conditioning is standard and its value has been fully demonstrated in terms of efficiency and lowered morbidity. Among the references given in this section, papers by the following are especially recommended to the reader who desires to familiarize himself with the general problems of temperature, humidity, and climate. Bazett (*878*) 1948 and (*879*) 1949; Critchley (*994*) 1946; Gagge and Herrington (*889*) 1947; Grant (*891*) 1951; Hardy (*892*) 1950; Herrington (*894*) 1949; Herrington and Hardy (*895*) 1949; Lee (*899*) 1948; Saunders (*907*) 1951; Spealman, Newton, and Post (*909*) 1947; Spealman, Yamamoto, Bixby, and Newton (*910*) 1949; and Yaglou, Baetjer, Machle, McConnell, Shaudy, Winslow, and Witheridge (*912*) 1950. A study of these reports and others given in this Sourcebook on heat and humidity problems indicates that our knowledge of the physiology and pathology of heat and humidity is quite

comprehensive. From the point of view of submarine medicine, the important consideration at this time is the application of this knowledge.

877. Adolph, E. F. Acclimatization to heat and cold. pp. 488–496 in: Part IV. Physiology in: *Advances in military medicine, Vol. II.* Edited by E. C. Andrus, D. W. Bronk, G. A. Carden, Jr., C. S. Keefer, J. S. Lockwood, J. T. Wearn, and M. C. Winternitz. Boston, Little, Brown and Co., 1948, 472 pp. [R]

878. Bazett, H. C. Human efficiency as affected by climate and its relation to social development. *Advanc. Sci.,* 1948, *4:* 348–353.

879. Bazett, H. C. The regulation of body temperatures. pp. 109–192 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp. [R]

880. Bean, W. B. Treatment of conditions incident to hot climate. pp. 4–385—4–399 in: *Treatment in general medicine.* Volume 4. Edited by Hobart A. Reimann. Fourth edition. Philadelphia, F. A. Davis Co., 1948, 776 pp.

881. Bedford, T. *Environmental warmth and its measurement.* 1946, London, H. M. Stationery Office, 40 pp. Abstr: *Bull. Hyg., Lond.,* 1946, *21:* 595–596. [R]

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883. Buettner, K. Effects of extreme heat on man. II. Analysis of temperature changes caused by different kinds of heat application to the skin. USAF. Randolph Field, Texas. School of aviation medicine. *Project 21–26–002, Rept. no. 2,* November 1951, 10 pp.

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887. Edwards, J., Jr. Electroencephalographic study of men transferred from the subtropic to the subarctic. USAF. Ladd air force base, Alaska. Arctic aeromedical laboratory. *Project 21–01–004, Section IV,* December 1950, 18 pp. [P]

888. Fischer, A., S. Gerö, I. Rózsahegyi, and C. Sellei. Munkaártalmak pathogenesise és megelözése. [General study of pathogenesis of disturbances in high temperature exposures.] *Orv. hetil.,* 1949, *90:* 452–456. [P]

889. Gagge, A. P. and L. P. Herrington. Physiological effects of heat and cold. *Annu. Rev. Physiol.,* 1947, *9:* 409–428. [R]

890. Glaser, E. M. Acclimatization to heat and cold. *J. Physiol.,* 1950, *110:* 330–337. *Abstr. World Med.,* 1950, *8:* 5–6. [P]

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892. Hardy, J. D. Physiological responses to heat and cold. *Annu. Rev. Physiol.,* 1950, *12:* 119–144. [R & P]

893. Hardy, J. D. and G. F. Soderstrom. Heat loss from the nude body and peripheral blood flow at temperatures of 22° to 35° C. *J. Nutrit.,* 1938, *16:* 493–510. [P]

894. Herrington, L. P. The range of physiological response to climatic heat and cold. pp. 262–276 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

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904. Mole, R. H. The relative humidity of the skin. *J. Physiol.,* 1948, *107:* 399–411. [M]

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B. TEMPERATURE AND HUMIDITY PROBLEMS ON SHIPBOARD AND IN SUBMARINES

Prior to the installation of air-conditioning machinery in submarines, high temperature and humidity constituted important limiting factors in efficient performance of combat duty. The submarine is a weapon of aggressive warfare and its chief function is to deliver torpedoes to enemy targets in the most efficient manner. Thus it is imperative that only such equipment be installed on board a submarine which will contribute to the carrying out of its military mission. Therefore, provisions which increase the habitability of the submarine from the human point of view must be judged in the light of overall military efficiency. Without adequate air cooling and ventilation, habitability on an active war patrol may become so poor that material defects and decreased personnel endurance may compromise the effectiveness of the ship. The relationship of excess heat and humidity in the conning tower to the efficiency of control parties during long approaches to an enemy target is very important. For discussions of heat and humidity problems on shipboard and in submarines, the reader should consult the references listed below.

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C. PHYSIOLOGICAL EFFECTS OF RAISED TEMPERATURES

The following three references are given as source material on the general physiological effects of heat: Machle and Hatch (*980*) 1947, Wakim (*1024*) 1948, and Wezler (*1025*) 1950. The maintenance of a constant body temperature under conditions of raised temperature and humidity involves widespread functional adaptation throughout the body. These adjustments include an increase in skin temperature, increase in evaporation of sweat, and increase in cardiovascular and respiratory activity. High humidity diminishes or abolishes the body's capacity to give off heat by evaporation. The skin temperature rises steadily with rising air temperature, though at a gradually decreasing rate. This rise in skin temperature is affected by dilatation of cutaneous vessels, including the arteriovenous anastomoses. As the body temperature rises, there is an increase in pulse rate, stroke and minute volumes of the heart, and cardiac work. The increase in heart rate is estimated at 10 beats for every degree Fahrenheit rise in body temperature. This, however, is extremely variable. Under some circumstances, there may be a decrease of stroke volume of the heart with increase in heart rate. The blood pressure may rise or there may be a fall in diastolic pressure with no change in systolic pressure. Skin vasodilatation may be due to the stimulation of axon reflexes in the skin, liberation of vasodilator metabolites, and warming of the blood to the hypothalamus-evoking vasodilatation of central nervous origin. It has been estimated that there is an increase in respiratory rate of 5 to 6 respirations per minute for every degree Fahrenheit rise of body temperature. This varies widely in unacclimatized persons. Metabolic activity may increase during hyperthermia and the respiratory volume increases. Overheating may result in heat collapse, heat stroke, or heat cramps. In heat collapse, there may be no rise in body temperature and the symptoms are mainly

those of hemodynamic failure. There is pallor, poor venous return, and rapid heart action. The condition is mainly reversible. In heat stroke there is elevation of body temperature and symptoms associated with organic changes, especially in the brain. Heat cramps are caused by loss of water and chloride in blood and tissues, especially in the central nervous system. There are tonic and chronic spasms, mild tetany, and twitching, with elevated leukocyte count, hemoconcentration, reduced serum sodium and chloride levels. Death from heat can occur as soon as the changes resulting from overheating, especially those in the brain, become irreversible.

For further studies on general physiological problems of hypothermia, papers by the following are cited: Bedford, Mackworth, McArdle, and Weiner (*932*) 1948; Carpenter (*938*) 1948; Glickman, Inouye, Keeton, and Fahnestock (*952*) 1948; Gt. Brit. MRC–RNPRC, HS (*957*) 1946; Gt. Brit. MRC–RNPRC, CES (*958*) 1949; Houghten, Gutberlet, and Ferderber (*961*) 1943; Humphreys, Imatis, and Gutberlet (*962*) 1946; Humphreys, Imatis, and Gutberlet (*963*) 1946; Imrie (*964*) 1950; Marbarger and Taylor (*984*) 1946; McArdle, Dunham, Holling, Ladell, Scott, Thomson, and Weiner (*989*) 1947; Pace, Fisher, Birren, Pitts, White, Consolazio, and Pecora (*1002*) 1945; Shelley and Horvath (*1018*) 1946; Spealman (*1019*) 1945; Taylor (*1021*) 1947; and Taylor and Marbarger (*1022*) 1946.

Generally speaking, hyperthermia increases the activity of sense organs, peripheral nerves, and the central nervous system. The pain threshold temperature of the human skin irradiated with strong infrared radiant heat was found to be 44.8° C. by Buettner (*935*) in 1951. Marechaux and Schafer (*985*) 1950 reported on the temperature sensitivity of different parts of the body tested in a climate chamber. With increasing temperature, the warm sense sets in, in characteristic sequence from the upper to the lower parts of the body. With decreasing temperature, it disappears in the reverse order, first in the feet and last in the forehead. Typical of the studies of the effect of temperature on nerve activity is a report by Engelhardt (*946*) 1951 on the effect of temperature changes on conduction velocity in the sciatic nerve of frog and cat.

As Rothstein and Towbin (*1014*) 1947 have stated, one of the important functions of the circulatory system is the transport of heat from within the body to the surface. The rate of heat transfer depends upon the rate of blood flow to the skin and the temperature gradient between the internal organs and the skin surface. In the cardiovascular response to heat, it is more efficient to maintain a given cardiac output with a slower pulse and a larger stroke volume than with a faster pulse and a smaller volume. Such a shift represents a slow adjustment to the task of increased cardiac output imposed by heat and may be an important factor in the acclimatization to heat, for in the unacclimatized subject the pulse rate increases considerably and it is likely that in some subjects the stroke volume diminishes. An outstanding response to hyperthermia may be dehydration with loss of fluid from the blood. This imposes an additional cardiovascular strain, additive to the peripheral vasodilatation caused by heat. This is balanced to an unknown extent by constriction in other vascular areas. With increased loss of water, the concentration of red blood corpuscles per unit volume of blood increases as does the plasma protein concentration. There is an increase in blood viscosity and the heart expends more energy to pump a given amount of blood. Dehydration in the heat is accompanied by increase in pulse rate and rectal temperature. The stress of dehydration is partitioned between cardiac strain as evidenced by pulse-rate increase and a storage of heat as evidenced by increased rectal temperature. Pulse-rate and rectal-temperature increases are good indicators of total circulatory strain, one of the limiting factors in man's performance in heat.

For further studies of the cardiovascular responses to heat, papers by the following should be consulted: Cooper and Kerslake (*940*) 1948; Glaser, Berridge, and Prior (*951*) 1950; MacPherson (*981*) 1946; MacPherson (*982*) 1946; Miller and Moor (*993*) 1947; Roos, Weisiger, and Moritz (*1013*) 1947; and Scott (*1017*) 1945.

Johnson (*965*) 1943 has shown that in subjects with normal, healthy cardiovascular systems the peripheral circulation is maintained or even increased in the presence of dehydration with hemoconcentration due to exposure to heat. Evidence exists that generalized vasodilatation in the periphery occurs in response to afferent nerve stimuli arising in locally heated areas of the skin. Further evidence supporting this hypothesis has been obtained by Cooper and Kerslake (*941*) 1949 by heating the chest and abdominal skin under a radiant heat cradle. The hand blood flow increased, the rise commencing within 12 seconds of switching on the lights. The time of onset of this dilatation was independent of the resting hand blood flow and of the intensity of the illumination within wide limits. Heating the front of the legs caused a similar increase in hand blood flow with the same time relations. This response was unaltered when the circulation to the legs was arrested. The peripheral vasodilatation was found to be associated with a fall

in mouth and rectal temperatures. Mead and Schoenfeld (*992*) 1950 reported mean blood flow in the vasodilated finger of five individuals, seated in an uncomfortably warm environment, ranging from 115 cu. cm. to 142 cu. cm. per 100 cu. cm. of tissue per minute. In one subject further warmed in a bathtub, a mean value of 173 cu. cm. per 100 cu. cm. of tissue per minute was obtained. In vasodilated fingers, both arterial and venous flow were shown to be markedly pulsatile in character. This character of the venous flow in the vasodilated finger is consistent with the flow through structures such as the arteriovenous shunts known to be present in the finger. In a report on the reactions of the peripheral circulation to external heat, Grayson (*955*) 1949 measured finger blood flows, forearm blood flows, and skin temperatures on healthy human subjects under varying conditions of environmental temperature. Finger blood flows and forearm blood flows were estimated separately to distinguish between vascular reactions of skin and muscle. The response of the skin circulation to rising environmental temperature consisted of (1) an increase in skin blood flow as the environment warms to approximately 36° C.; (2) a decrease in skin flow as the environment rises in temperature from 36° to 40° C.; and (3) an increase in blood flow as the environmental temperature rises above 40° C. During the phases (1) and (2) the body temperature remained steady or fell and there was no change in muscle blood flow. During the phase (3) the body temperature rose and there was an increase in forearm blood flow with the onset of perspiration. The vasoconstriction occurring in the skin when the environmental temperature rose above 36° C. was regarded as a possible temperature regulating mechanism. The author stated that forearm blood flows do not respond to environmental temperature increases until the body temperature has begun to rise. Barcroft, Bonnar, and Edholm (*930*) 1948 made observations on blood flow in human subjects on normal forearms, sympathectomized forearms, on forearms with the skin flushed by mustard, and on those with the skin blanched with adrenalin. Body heating by putting both feet in hot water for a maximum of 50 minutes increased the blood flow in the forearm from 3.1 to 9.3 cu. cm. per 100 cu. cm. of forearm per minute. Since the effect was absent in sympathectomized forearms, the vascular reflex was held to have been mediated by the sympathetic nerves. Flushing of the forearm skin produced by mustard increased the forearm blood flow to the same extent as body warming. Since, however, in these experiments, the body warming did not flush the skin it was likely that the heat vasodilatation was for the most part deep to the skin. Body warming increased the blood flow in the forearm when the skin blood vessels were intensely constricted by adrenalin. It was concluded that the dilatation was for the most part deep in the skin, most probably in the skeletal muscle.

The effect of thermal stimuli on the circulation in the human colon has been studied by Grayson (*956*) 1949. The subject was a patient with a colostomy performed about 9 months previously. Needle thermocouples, inserted into a small knuckle of bowel exposed on the surface of the abdomen, recorded temperature changes in response to general body heating and to thermal stimuli applied to the abdominal wall near the colostomy. Skin-temperature changes from an index finger were recorded for purposes of comparison. A cold, ether-soaked pad applied to the abdomen produced a marked rise in colonic tissue temperature, whereas a hot pad produced a definite fall. These responses were abolished by the surface application of novocaine to the colostomy. Cold applied to the colostomy itself was found to produce a generalized vasodilatation throughout the exposed tissue. Generalized body heating causes a vasoconstrictor response in the colon during the early stages of body heating followed by a vasodilator response after prolonged body heating. The vasoconstrictor phase in the colon accompanies an increase in cutaneous blood flow, whereas the vasodilator phase appears only after the rectal temperature has risen.

For further studies on vasomotor response to heat, papers by Ebaugh and Thauer (*944*) 1950 and Leusen and Demeester (*979*) 1951 may be consulted.

For a discussion of temperature extremes and water and salt lacks, a chapter by Bartley and Chute (*931*) 1947 may be consulted. Three papers on water and salt depletion which appeared in 1947 by Marriott (*986, 987* and *988*) constitute a very complete discussion of the subject. As Brown and Towbin (*933*) 1947 have stated, a water deficit of 3 percent of body weight or an air temperature of 24° F. above average skin temperature increases man's circulatory strain as much as does work which involves energy expenditure of twice the basal rate. The maximal rate of energy expenditure which man can endure depends directly on the air temperature and upon his body-water content. A working rate which is comfortable for a man in water balance becomes intolerable when he has attained sufficient dehydration. An increase of 10° F. air temperature is stated by the authors to increase man's circulatory

strain as much as an energy expenditure of 29 calories per square meter of body surface per hour. A dehydration of 1 percent of body weight increases circulatory strain as much as an energy expenditure of 24 calories per square meter of body surface per hour and an exposure to a temperature of 110° F. necessitates a 25 percent reduction in his working rate. A body-water deficit of 2.5 percent requires the same reduction of work output. According to Adolph (*928*) 1947, men who lose 1 to 11 percent of their body weight by rapid sweating in simulated desert conditions show a loss in volume of circulating plasma. As measured by the method of dye dilution, the plasma volume diminishes 2.5 times as much as does an equal volume of the whole body. This decrease of plasma volume is paralleled by an increase in total serum concentration. For a further report on water loss in human subjects due to increased temperature, a paper by Brumsteyn (*934*) 1950 may be consulted. Papers by McLean, Moritz, and Roos (*991*) 1947 and Pincus and Elmadjian (*1003*) 1946 contain data on blood changes caused by cutaneous exposure to excessive heat and the lymphocyte response to heat stress in normal and psychotic subjects. Changes in blood gas equilibria resulting from exposure to hypothermia have been reported by Gordon, Darling, and Shea (*953*) 1949.

Exposure to elevated temperatures affects the gastric emptying time in both animals and men. Cordier and Piery (*942*) 1950 found that in male albino rats fasting 48 hours an increase of environmental temperature from 18° to 45° C. reduced the rate of passage through the stomach and delayed gastric emptying by an amount proportional to the temperature increase. Increase of external temperature from 18° to 40° C. did not appreciably affect the rate of absorption of glucose in the same animals. In 17 normal young men the gastric empyting times were observed at rest at environmental temperatures of 77° and 120° F. by Henschel, Taylor, and Keys (*960*) 1943. In all but one of the subjects the gastric emptying time was faster at the higher temperatures. Twelve of the subjects showed an average decrease of 30 percent in gastric emptying time when the temperature was 120° F. Observations carried out on about 100 normal men during hard work at 120° F. failed to indicate any lack of appetite or any sign of decreased activity, except in actual heat exhaustion. Regarding food intake by healthy, physically fit soldiers in desert and jungle areas, Johnson and Kark (*966*) 1947 found that personnel tended to choose a diet with a lower caloric value at an environmental temperature of 92° F. This is contrasted to higher caloric diets chosen by personnel in Arctic environments as low as −30° F. The authors stated that the caloric expenditure for a given task is greater in cold than in warm climate because of the hobbling effect of Arctic clothing and equipment. Also more heat is required in cold than in warm environments to maintain thermal equilibrium. The percent of protein chosen is approximately the same in all environmental conditions. According to Kark, Aiton, Pease, Bean, Henderson, Johnson, and Richardson (*969*) 1947, the most important considerations in troop feeding are variety of the food items, similarity to those the soldier usually eats in ordinary life, avoidance of caloric deficits, and high acceptability insured by good food preparation. Tables of representative values of foods commonly used in tropical countries have been prepared by Platt (*1005*) 1945.

From an experimental study of the effect of nutrition upon the reactions of animals to heat, Robinson and Lee (*1008*) 1947 concluded that the caloric value of the diet has a significant and at times practically important effect on the reactions of animals to hot conditions. However, the proportion of protein in the diet is not significant. Mitchell and Edman (*994*) 1951 have called attention to the conclusion from animal experiments that in hot environments the requirement for thiamin is markedly increased, while the riboflavin requirement is decreased. The requirement for ascorbic acid may be increased if the body temperature is raised. These authors have pointed out that animal experiments constitute an insecure guide to human needs. Direct and field observations on human subjects show that the energy requirements are decreased in hot climates due to diminished basal expenditure of energy or greater efficiency in certain types of muscular work, lighter clothing, lessened capacity or motivation for work. The water requirements are increased with sweating and in proportion to the amount of sweat, whereas the daily water requirement in temperate climate may be 2½ to 3 liters. This will increase to 13 liters or more in a hot environment. Water losses must be covered by water intake at frequent intervals and thirst is not an adequate guide to water requirement. The salt requirement may be increased from a daily intake of 2 to 5 grams up to 15 to 17 grams under profuse sweating. This large increase in salt requirement is stated by the authors to be confined to the period of acclimatization. The authors believed that in acclimatizated individuals the salt replacement provided in food at meals is adequate. They consider that salt tablets are unnecessary except in unusual situations prior to acclimatization. There is no statistical evidence that men voluntarily select

low-protein diets in hot climates and the authors consider that there is no benefit to body heat economy from a low-protein diet. The protein requirement may actually be increased slightly in the tropics. The vitamin requirements are stated not to be appreciably increased by residence or work in tropical climates. In hot environments, the requirement for iron and perhaps calcium is increased. The authors feel that attempts to increase tolerance or accelerate acclimatization by dietary modifications have not been as extensive as the importance of this problem warrants. In provision of rations for troops in the tropics, they stress the importance of a considerable variety of foods, items which the soldiers are accustomed to in ordinary life, but with emphasis on those of high biological value. A proper packaging and storing is important in preserving nutritional factors, particularly the vitamins.

Pertinent to problems of nutrition and water intake in man in environments at high temperatures is the question of thirst. Adolph and Wills (*929*) 1947 have reviewed the current theories about the mechanisms of thirstiness. They found that increasing saliva flow did not give to the dehydrated man a sense that he had drunk water, nor did reducing his feeling of fatigue allow him to behave as if he had a normal body-water content. The authors concluded that, in practice, theories regarding thirst have proven useless. New theories are required. These must be so specific that they will show us how to cheat the body and so relieve some of the mental and physical distresses of thirst. They concluded that measures other than taking in water were not successful in improving the state of the dehydrated man, nor in relieving the urge to drink water. There is really no known substitute for water.

There is an extensive amount of literature on water balance and sweating under conditions of high temperature, with or without elevated humidity. A representative study is that carried out by Nelson and Bean (*997*) 1942. Using 56 enlisted men living in a hot room of the laboratory, temperatures were maintained at 120° F. during the day and at 90° F. at night. Daily water requirements were found to be contingent upon the environmental temperature and the severity of physical work. Water requirements, therefore, varied with the duties of the troops and the environment. In a hot climate, man dissipates the greater proportion of his heat by evaporation of sweat. Failure to supply sufficient water to make up for the loss in sweating results in depletion of body water. If continued, this leads to progressive loss in weight, physical deterioration, and reduced efficiency and capacity for work, and greatly impairs morale and motivation. Reduction of water consumption to levels below that required to maintain water balance will be followed by incapacitation, whether the reduction is gradual or abrupt. Schedules which require that a man disregard thirst and drink only at mealtimes results in no saving of water and may cause discomfort and reduced physical importance. Thirst is stated by the authors to be an inadequate indicator of rapid tissue dehydration at high rates of sweating which accompany even moderate work in heat. At high temperatures men will consistently drink less water than they are losing in sweat. Augmenting the water intake so as to balance the fluid lost in the sweat will increase the amount of work which can be done and reduce injurious effects. It has been found that the daily water requirement is not significantly changed as men become acclimatized to heat. Regarding salt requirements, the authors have stated that the requirement for salt is in direct proportion to the amount of water taken. With exposure to heat, the need for extra salt is greater during the early drop than after acclimatization is established. The authors recommended that for light work 4 quarts of fluid per day be taken at 95° F., 6 quarts per day at 105° F., and 10 quarts at 115° F. For moderate work, the requirements are 5 quarts a day at 95° F., 7 quarts at 105° F., and 11 quarts at higher temperatures. For strenuous work, 7, 9, and 13 quarts are required for the respective temperatures. In a study on human subjects by Mitchell, Hamilton, and Shields (*995*) 1943, 4 men were subjected to 24 consecutive weeks of observation. Two conditions were studied: (1) 112° F. with 20 percent humidity, and (2) 100° to 102° F. with 76 percent humidity. The authors concluded that sweating under hot, moist conditions is much more profuse and much more variable than under hot, dry conditions and is associated with a much greater increment in rectal temperature. The sweat under the humid conditions, besides being more profuse, has a higher concentration of salt than the sweat excreted under the dry conditions. A man may lose an equivalent of 23 grams of salt daily under hot, moist conditions and only 5.25 grams under hot, dry conditions. Sweat produced under muscular activity conditions is also more concentrated than that produced during repose. The rate of sweating is greatly increased by even a moderate degree of muscular work. Ascorbic acid is not secreted in appreciable concentrations in human sweat, even when the tissues and fluids of the body are physiologically saturated with vitamins. The loss of thiamin in sweat is minimal under

all conditions of activity and environment, averaging only 0.2 microgram per hour. The average losses of nicotinic acid and riboflavin in sweat vary from 7 to 29 micrograms per hour and 0.9 to 6.6 micrograms per hour, respectively, and parallels the rate of sweating. Under conditions of excessive sweating of 1 liter per hour, the sweat may contain considerable quantities of thiamin, riboflavin, nicotinic acid, iron, and calcium. For further studies on the physiology of sweat formation, papers by the following authors may be consulted: Adolph (*927*) 1947, Burch (*936*) 1948, and Ladell (*976*) 1947–48. For studies on the rate of sweating, the following references are useful: Gerking and Robinson (*948*) 1946; Gosselin (*954*) 1947; MacPherson and Lee (*983*) 1948; Randall and McClure (*1007*) 1949; Robinson (*1009*) 1947 and (*1010*) 1949; Sato, Kikuta, and Hisao (*1016*) 1950; and Thomson (*1023*) 1948.

A number of studies are available on salt concentration of sweat and factors influencing chloride excretion in sweat. Johnson, Pitts, and Consolazio (*967*) 1944 reported that in adequately nourished men under hot conditions the chloride in sweat increases as work is prolonged. There are definite individual differences, and the sweat chloride is decreased by drinking water during work. It is still further decreased by administration of an equal volume of saline instead of water. It increases as the rate of sweating increases. It is independent of acclimatization and increases with increasing body temperature. It also increases with local skin temperature and is independent, within limits considered normal, of the plasma protein and plasma chloride. Ladell (*975*) 1945 stated that there was a great variation in chloride concentration of sweat in the same subject and in different subjects. The chloride concentration of the sweat was stated to increase with the duration of sweating and with the rate of sweating. The sweat, however, was always hypotonic. With salt deficiency, the chloride concentration of sweat was reduced. In 1948, Ladell (*978*) measured the chloride content of whole body sweat as well as the chloride concentration of sweat samples obtained from an arm totally enclosed in a bag. These latter values were found to be the same as for whole body sweat. This did not indicate to the author that the chloride concentration in sweat is the same for all parts of the body. Johnston, Conn, Louis, and Steele (*968*) 1946 found that in men, fully acclimatized to heat and working sufficiently hard to produce 5 to 10 liters of sweat in 24 hours, reasonably accurate balance studies for chloride can be made when the averages of the daily concentration of salt in the hand sweat is used to represent the concentration in the total body sweat for the period. Given sufficient chloride in the diet to insure chloride equilibrium under these conditions, the authors predicted the average concentration of chloride in body sweat for the period studied by applying the following formula: Total chloride intake minus total urinary chloride, divided by total sweat volume, equals average concentration of chloride in body sweat. When the predicted value for concentration of chloride in all of the body sweat produced in the period was compared with the determined value, good agreement was obtained. For further studies on the pattern of chloride excretion, papers by Robinson, Gerking, Turrell, and Kincaid (*1012*) 1950 and Kenney and Miller (*972*) 1949 may be consulted.

Ladell (*977*) 1947 has carried out studies on creatinine losses in the sweat during work in hot, humid environments. These tests were conducted on 4 young men fully acclimatized to work under the environmental conditions of the experiment. Each exposure lasted for 160 minutes in an air-conditioned chamber kept at a dry bulb temperature of 100° F. (wet bulb, 93° F.); the relative humidity was 77 percent, the air movement was below 50 feet per minute. The subjects were completely nude, except for a bag completely covering one arm in which the sweat was collected. Whereas the creatinine content of both saliva and blood increased threefold after an oral dose of 5 grams of creatinine, there was only a slight increase in the creatinine content of the sweat. The sweat creatinine appears to be more closely linked with the rate of sweating than with the level of creatinine in the blood. Statistically, the author found a good correlation between the reciprocal of the sweating rate and the sweat creatinine. This relationship between creatinine content and sweating rate is the opposite of that observed for chloride concentration in sweat. It has been reported that the greater the sweating rate the more nearly does the chloride content of sweat approach that of plasma. It would appear to the author that there are at least two mechanisms involved in the production of sweat from the body fluids. Some similarity between the mechanisms of sweat formation and urine formation has been suggested, but the fact that the creatinine content of sweat is little affected by that of blood, whereas the urinary creatinine is greatly affected by blood creatinine concentration, indicates that the mode of production of the two fluids must be very different.

For further studies on sweating and water balance, papers by the following may be consulted: Molnar, Towbin, Gosselin, Brown, and Adolph

(*996*) 1946; Chin (*939*) 1950; Sato, Fukuyama, Sakal, Naito, Katayama (*1015*) 1950; Kawahata (*970* and *971*) 1950; and Kuroda (*973* and *974*) 1947.

From a large source of literature on temperature regulation and thermal balance under hot conditions, papers by the following authors have been selected: Friedrich (*947*) 1948; Glaser (*949*) 1949; Glaser (*950*) 1949; McCutchan and Taylor (*990*) 1950; Nelson, Eichna, Horvath, and Shelley (*998*) 1946; Nelson, Eichna, Horvath, Shelley, and Hatch (*999*) 1947; Nelson, Shelley, Horvath, Eichna, and Hatch (*1000*) 1948; Robinson and Gerking (*1011*) 1947; and Woodcock, Pratt, and Breckenridge (*1027*) 1952.

For a study of heat production and energy requirements of tropical people, a paper by Cullumbine (*943*) 1950 should be consulted. In these studies the basal heat production of 225 Ceylonese, males and females of various ages, was determined.

The response of the endocrine glands to heat stress is a matter of importance and one which has been subjected to much experimental investigation. One such study is that carried out by Stein, Bader, Eliot, and Bass (*1020*) 1948. Three healthy, white males were exposed successively, after a preliminary 2 weeks period of physical conditioning, to nineteen, five, and one 15-minute period of heat at a dry bulb temperature of 107° F. (wet bulb, 89° F.). They were then subjected to fourteen 5-hour periods of cold at 20° F. and following this to five reexposures to heat, and then to a 5-week interval of no exposure to environmental stress or rigorous exercise. Finally, there were three reexposures to heat. Measurements were made of the circulating eosinophile count, the absolute lymphocyte count, the urinary uric acid-creatinine ratio, the 24-hour 17-ketosteroid excretion, and the effects of administration of ACTH to evaluate adrenal cortical responses. Basal metabolic rates were studied as an indication of thyroid activity. The number of circulating eosinophiles was significantly reduced in daily counts during exercise, a combination of heat and exercise, and a combination of cold and exercise as compared to a baseline period without stress. There was no significant difference in the excretion of 17-ketosteroids in any of the experimental periods. This was also true of the daily urinary uric acid-creatinine ratio, and the absolute lymphocyte count. Administration of ACTH for the assessment of adrenal cortical function yielded the same pattern of response after heat and cold stress as after control experiments. This indicated to the authors that this method is not sufficiently sensitive for this type of study. There was no significant change in the basal metabolic rate throughout the experimental period in any of the subjects.

It is well known that high temperatures depress or inhibit spermatogenesis in the testes. An experimental study reported in 1950 by Elfving and Turpeinen (*945*) reveals that immersion of the scrotum of rats in water at 40.4° C. for 3 hours has no effect upon the production of spermatozoa. Temporary sterility is produced by immersion at this temperature for 5 to 8 hours. Immersion at 42.4° C. for 30 minutes produces temporary sterility and for 45 minutes produces permanent sterility. The animals tolerated a temperature of 46.3° C. for 5 minutes with no effect, while exposure for 8 minutes produced temporary sterility and exposure for 15 minutes resulted in permanent sterility. The effects of the heat treatment on the testicular hormone production were also studied using the weight of the seminal vesicles as an indicator for the presence of androgens. A 20-minute exposure to 44.3° C. had no appreciable effect on the vesicle weight. After an exposure to 46.3° C. for 20 minutes, a definite fall in the weight of the seminal vesicles was found 1 week after treatment. The vesicles, however, recovered rapidly and 1 week later had almost returned to their normal weight. It is evident from these studies that the endocrine function of the testis is considerably more heat resistant than is spermatogenesis.

Regarding the effects of environmental heat stress on renal functions, a paper by Radigan and Robinson (*1006*) 1949 may be consulted.

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D. TOLERANCE AND ACCLIMATIZATION TO HEAT AND HUMIDITY

As Yaglou (*1070*) 1945 has stated, in several naval situations human tolerance to heat at various temperatures and humidities constitutes a limiting factor in operations. For short exposures, higher temperatures can be tolerated than for continuous exposures. For the latter, at a relative humidity of 100 percent, 90° F. is the maximum dry bulb temperature tolerable. At a relative humidity of 20 percent, a dry bulb temperature of 116° F. has been fixed as the maximum. Yaglou defined the heat-tolerable time as the time of exposure required to raise the mean pulse rate of a group of 5 subjects from an initial rate of 75 up to 125 beats per minute and the rectal temperature from an initial level of 99° F. to 101° F. Serious discomfort does not occur until the pulse rate exceeds 135. A pulse of 160 is quite distressing and collapse may occur if the pulse rate exceeds 180 beats per minute.

A series of reports by Blockley and associates (*1031, 1032, 1033,* and *1034*) on tolerance to extreme heat may be consulted. In the first of these reports, Blockley and Taylor (*1034*) 1948 exposed human subjects to air temperature levels of 100°, 140°, 160°, 180°, 200°, 220°, and 240° F. There was one exposure to 250° F. The average vapor pressure ranged from 0.25 to 0.9 in Hg. In most of the experiments the vapor pressure was about 0.8 in. Hg. The skin temperature rose during exposures, the rate of rise being greater with increased ambient temperature. A maximum skin temperature of 107° F. was reached at an ambient temperature of 240° F. in a subject wearing medium weight woolen clothing and cotton underwear. The heart rate increased in proportion to the skin temperature,

usually reaching 140 to 160 beats per minute. The maximum rate was 172 beats per minute. The blood pressure showed individual differences. The systolic pressure rose during exposure in all cases, but the diastolic pressure declined continuously in one subject and remained stable or slightly elevated in another. There were minor variations in the electrocardiogram during and after exposure to heat, but no distinct electrocardiographic indications of heart damage were noted. Rectal temperature changes were slight and slow of onset. The authors considered rectal temperature changes to be unreliable as an indication of the extent of temperature stress in short exposures. The highest rectal temperature recorded was 101° F. The maximum temperature of the exhaled air was recorded at 104° F. indicating that the mucous membranes exert a strong cooling influence. In these subjects, there was a feeling of air hunger associated with deep and irregular respiration. This was accompanied by restlessness and nervous irritability with waves of dizziness at the terminal stages. At an ambient temperature of 180° F. the mean tolerance time for 4 exposures was 49 minutes; at 200° F. the mean tolerance time was 33 minutes; at 220° F. the mean tolerance time was 26 minutes, and at 240° F. subjects showed a mean tolerance time of 23½ minutes. Of physiological variables measured, Blockley and Taylor (*1032*) 1950 considered the skin temperature constitutes the best single index of thermal strain. Blockley and Lyman (*1031*) 1950 have measured mental performance under heat stress as indicated by addition and number checking tests. These experiments were conducted at a vapor pressure of 0.8 in. Hg and at 3 levels of temperature; namely, 160°, 200°, and 235° F. The duration of each exposure was determined by the ability of the individual to tolerate the heat, and the work on the mental problems was continuous during the exposure except for a 15-second rest period in each 3 minutes. In two of the experimental environments, the performance in the final 6 minutes of heat exposure was found to be significantly poorer than in the preexposure period, but no significant differences were found for the 200° F. experiments. In a study of psychomotor performance of human subjects as indicated by a task simulating aircraft instrument flight, Blockley and Lyman (*1033*) 1951 conducted experiments at 160°, 200°, and 235° F. with a vapor pressure of approximately 0.8 in. Hg, using a comfortable environment in the neighborhood of 80° F. as a control. The subjects were given an initial 1-hour practice period on experimental flight patterns before the first heat exposure. The task consisted of continuous repetitions of this flight pattern, which was 4 minutes in duration and included 4 turns combined variously with climbs, dives, and level flight. Although differing in level of competency or skill in the task, no subjects showed a change in proficiency within 80 minutes of "flight" in the comfortable environment. On exposure to heat, however, there was striking deterioration of performance, commencing from 4 to 13 minutes prior to the termination of exposure.

Adolph (*1028*) 1946 pointed out that a practical limit to tolerance of high temperature is signaled by the premonition of circulatory collapse experienced by acclimatized subjects. Temperatures above 90° F. wet bulb can rarely be endured indefinitely. During work, the intolerable wet bulb temperature may be as low as 80° F. or less. There is an initial acclimatization in the majority of subjects which is nearly complete after 4 exposures of 2 hours each to limiting temperatures. There is a suggestion of additional slower acclimatization requiring a month or more. The variability in heat tolerances among individuals is reduced by their acclimatization.

Adolph (*1029*) 1947 has ascertained the tolerance times of dogs, cats, rabbits, guinea pigs, rats, and mice to warm dry air at various temperatures. A consistent sign of lethal conditions was found in the rectal temperature which had different median critical values for each species, lying between 41.7° and 43.4° C. Heat stroke appeared to result from hyperthermia that injured unidentified regulatory tissues. Death might be delayed for periods up to 26 hours after the animals had been sujected to critical rectal temperatures and then cooled. Dehydration through panting was limited in the mice, rats, rabbits, and guinea pigs, but was copious in the cats and dogs. Evaporation proceeded as rapidly after considerable dehydration as during periods of water balance. Dehydration resulted in a concentrated plasma and by inference a depleted plasma volume and limitation of circulation. This was considered important in sensitizing the animals to warm atmospheres. The explosive rise of rectal temperature was considered to develop through failure of the circulation to transport heat to the surface. Animals allowed an unlimited water intake did not drink enough to maintain body weight while in the hot atmospheres. If deprived of water they subsequently drank less than enough to recover body weight except in the case of dogs with water deficits of less than 9 percent of body weight.

Eichna, Ashe, Bean, and Shelley (*1045*) 1944 have determined the upper limits and the safe limits of temperature and humidity at which acclimatized normal young men can work. At wet bulb tempera-

tures below 91° F., men worked easily, efficiently, and with only mild physiological changes. At wet-bulb temperatures from 91° F., and 94° F., prolonged moderate hard work was rather difficult, resulting in loss of vigor and alertness, undesirable physiological responses, and occasional illness. Moderately hard work at wet-bulb temperatures of 94° F. or higher rapidly lead to total disability in most men. Approximately 1 hour of sustained work was tolerated by most subjects, while those who worked longer did so inefficiently and with functional disturbances. Hatch (*1050*) 1945 has pointed out that resting human subjects can tolerate dry heat well above 200° F., providing the duration of exposure is very brief. Ellis (*1049*) 1950 has reported that experimental work has in general supported the provisional recommendation for British sailors of an effective environmental temperature of 86° F. as the upper tolerable limit in any compartment occupied for long periods of time. Ellis suggested that the effective temperature scale is inaccurate at higher levels of heat. For exposures of a few hours duration, skill deteriorates at levels of heat well below those at which men may carry out unskilled heavy work without loss of efficiency.

For reports on measures for improving tolerance to high temperatures, papers by the following may be consulted: Bock (*1035*); Johnson, Pitts, and Consolazio (*1052*) 1943; Mills, Cottingham, and Taylor (*1057*) 1947; Napier (*1058*) 1946; and U. S. OSRD–NDRC (*1068*) 1943.

Additional studies of tolerance to high temperatures are provided by the following authors: Burch and Sodeman (*1036*) 1944; Canada, Medical Intelligence Division, Ottawa (*1037*) 1945; Carpenter (*1038*) 1946; Consolazio, Pecora, and Pfeiffer (*1042*) 1944; Lee and MacPherson (*1054*) 1946; Mac Donald and Wyndham (*1055*) 1950; Taylor (*1064*) 1945 and (*1065*) 1946.

In a laboratory study of acclimatization to high temperatures, Eichna, Bean, and Ashe (*1046*) 1943 subjected 55 young enlisted men to dry-bulb temperatures ranging from 89° to 93.5° F. and relative humidities from 90 to 100 percent. In these studies carried out over a period of 6 months, it was found that soldiers exposed to moist heat became adapted by a process of acclimatization which enabled them to work more efficiently and with less risk of illness from heat than when first exposed. A man acclimatized to humid or dry heat can work with a lower body temperature, lower heart rate, more stable blood pressure, and less discomfort than when not acclimatized. The rapidity of acclimatization varies from 3 to 10 days. Men in good physical condition acclimatize more rapidly and are capable of greater amounts of work than those in poor condition. For complete acclimatization, work in humid heat is necessary. The capacity to perform a maximum amount of work in hot environments is most quickly attained by beginning work at a low level and increasing it within the tolerance of the subject as heat exposure continues. Strenuous work on initial exposure to heat is not well tolerated. Acclimatization to desert environments increases ability to work in humid heat. The authors recommend an acclimatization period of 2 weeks for troops with progressively increasing amounts of work and enough water to satisfy thirst. Alcohol should be prohibited. Eichna, Park, Nelson, Horvath, and Palmes (*1047*) 1950 studied acclimatization in an environment of 50.5° C. dry bulb and 15 percent relative humidity over a period of 10 days. The subjects carried out measured amounts of work. At the beginning of the acclimatization period, the heart rate increase was 59 beats per minute above the mean rate in a cool environment, whereas at the end of the 10th day it was only 15 beats per minute above the mean rate. The rectal-temperature increase at the beginning of the experiment was 1.2° C., but only 0.1° C. at the end of the experiment. The authors believe that acclimatization is mainly effected by an improvement in the loss of heat from the body by evaporation which lowers substantially the deep tissue temperature and reduces the cardiovascular burden imposed by the heat. Calorimetric measurements and clinical observations were made by Park and Palmes (*1059*) 1947 on three men working with a metabolic load of 180 calories per square meter per hour in a very dry, hot environment. On beginning work, deep and peripheral tissue temperatures rose rapidly owing to the retention of metabolic heat, as well as to heat gains by radiation and convection. The heavy load on the circulation probably accounted for many of the symptoms in the unacclimatized state. The principal thermal adjustment in the process of acclimatization was the development of a higher rate of sweat secretion. With acclimatization, signs of circulatory stress diminished greatly. The heat content of the body after acclimatization remained high, but the heat was absorbed in the peripheral tissues and the critical deep tissue temperature was maintained at a nearly normal value. Observations of Ladell (*1053*) 1950 indicated that acclimatization to work in moist, tropical heat is associated with increase in sweat production. For a study of individual variability in capacity to acclimatize to high temperature, a report by Taylor, Metz, Henschel, and Keys (*1066*) 1951 may be consulted.

Acclimatization to heat is essentially related to improved cardiovascular efficiency. This is indicated by a report of Adolph (*1030*) 1949 who observed diminution of the frequency of the pulse during acclimatization. Enhanced cardiovascular and muscular efficiency in acclimatization are also reported by Critchley (*1043*) 1945. Robinson (*1060*) 1949 stated that after 6 or 8 days of work in hot environments a man can work in thermal equilibrium under conditions in which it would be impossible for him to continue unless acclimatized. Rectal temperature and metabolic rate were found to return to normal levels after few days of exposure. There is an increase in circulating blood volume and the maximal blood flow to the skin increases 10 to 25 percent. There is greater stability of the circulation in different postural stresses and an increase in the efficiency of sweating. If water intake is limited and the demand for sweating is increased, the kidneys may reduce the urinary output by 500 cu. cm. At first, the sodium chloride output of the kidneys is reduced, but later, normal output is resumed.

In a study of cross-acclimatization to heat and cold, Eliot, Stein, and Bader (*1048*) 1948 exposed healthy, young male subjects to nineteen 5-hour periods of heat (107° F. dry bulb, 89° F. wet bulb, and 3 miles per hour wind velocity), 14 five-hour periods of cold (−20° F., wind velocity 3 or 4 miles per hour), and 5 reexposures to heat. After 5 weeks without environmental stress, 3 more heat exposures were given. The most striking findings of these studies were those in men acclimatized to heat, loss of acclimatization was not accelerated by repeated cold exposures, as judged by cardiovascular and metabolic indices and subjective reactions. More rapid and effective vasoconstriction with successive cold exposures was demonstrated. Continuous diuresis and increased chloride loss were observed during the period of cold exposures, and these trends were only slowly reversed by reexposure to heat. No significant difference in basal metabolic rate was observed between the hot and the cold periods. Blood, plasma, and "available fluid" volume studies revealed no consistent changes during the hot or cold periods, but plasma protein and hematocrit values showed definite hemoconcentration in the cold hemodilution in the heat. It was not demonstrated that increased tolerance to cold results from any of the changes observed. These same findings were reported by Stein, Eliot, and Bader (*1063*) 1948.

In a study of the mechanism of acclimatization to heat, Conn (*1041*) 1949 has concluded that the major differences between unacclimatized and acclimatized men consists of an improved peripheral circulation and an enhanced ability to resist depletion of body salt in the acclimatized subjects. This second difference manifests itself mainly as a capacity to produce sweat which is much lower in its concentrations of sodium and chloride than in the unacclimatized subjects. Since, under conditions of work in the heat, the major loss of body salt occurs via sweating, this adjustment assumes primary importance. The author believes that the process of acclimatization to heat is linked with an increased secretion of the adrenocorticotropic hormone by pituitary gland and the resulting enhancement of production and liberation of adrenal cortical steroids. Under the conditions of the author's experiments the need for conservation of body salt constitutes, it is believed, the stimulus which activates the mechanism and raises the level of activity of the pituitary-adrenal axis. According to a report of Robinson, Kincaid, and Rhamy (*1062*) 1951, men were able to perform work in an environmental temperature of 50° C. at 15 percent relative humidity under controlled conditions, with and without administration of desoxycorticosterone. On first exposure, subjects exhibited a rise in heart rate, body temperature, metabolism, and sweat sodium chloride concentration. They underwent the normal course of acclimatization during 5 days of exposure. The only significant changes produced by desoxycorticosterone were higher concentrations of plasma sodium and lower concentrations of sodium and chloride in the sweat during the first 2 days of exposure.

For further studies of acclimatization to heat and humidity, papers by the following may be consulted: Christensen (*1039*) 1947; Clark (*1040*); Dreosti (*1044*) 1949; Horvath and Shelley (*1051*) 1946; Robinson, Dill, Wilson, and Nielson (*1061*) 1941; MacPhersen, Lee, and Furlonger (*1056*) 1947; U. S. NRC–CAM (*1067*) 1949; Winslow and Herrington (*1069*) 1949.

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E. EFFECT OF HEAT ON EFFICIENCY

Observations under conditions of operation in submarines and other naval vessels have generally shown that personnel operate more efficiently in correctly air-conditioned spaces. Many investigations have been designed to examine under controlled conditions the influence of heat and humidity on working capacity. Bean, Eichna, Ashe, Horvath, and Nelson (*1071*) 1943 in such a study exposed men for 4 months, with only 5 minutes leave from the chamber a day, to temperatures ranging from 120° F. during the day to 90° F. at night, the relative humidity range was from 15–22 percent. The subjects became adapted to the heat and were able to carry out their duties more efficiently than at the beginning. Acclimatization was begun at the first exposure, and most of the acclimatization was acquired by the fourth day. Men in good physical condition acclimatized more quickly, and it was found that work in the heat was an aid to acclimatization. Strenuous work on the first exposure to heat was not well tolerated and often resulted in disability. Eichna, Bean, Ashe, and Nelson (*1077*) 1945 found that there is a measure of cross-acclimatization between hot, dry and hot, humid environments. Performance of acclimatized men in humid heat is impaired most seriously by lack of adequate water intake and lack of physical fitness. Performance is also effected adversely, but not so severely by lack of rest and sleep, by added clothing equipment, by alcohol intake, and by prolonged periods of work.

In a study of the effects of the thermal environment on working capacity among Indian workers in the Kolar gold mine, Caplan and Lindsay (*1074*) 1947 chose hand drilling as a performance test. The number of inches drilled per hour was taken as a quantative measure of performance. Six men of average fitness were acclimatized to a wet-bulk temperature of 93° F. Each test lasted 3 hours and the number of inches drilled was measured at the end of each hour. The performance during the first hour of work at a wet-bulk temperature of 83° F. was taken as 100 percent. In these studies it was found that at a wet-bulb temperature of 89.5° F. the performance was 80 percent during the first, second, and third hours. The same performance was found for wet-bulb temperatures of 88.2° and 86.6° F. Wet-bulb temperatures of 94.4°, 93.0°, and 91.3° F. were associated with a relative performance of 50 percent. In a normal working shift no serious diminution of work was found likely when the wet-bulb temperatures were below 85° F., but at 90° F. wet bulb temperature the relative performance over a 6-hour period was unlikely to be higher than 60 percent. It was considered that at 93° F. wet-bulb temperature it was improbable that any satisfactory work could be performed after the second hour and certainly not after the third hour. Macworth (*1081*) 1946 reported a study to determine if hot and moist atmospheres impair the accuracy with which trained telegraph operators can write down Morse messages heard over headphones. Eleven physically fit men ranging in age from 18 to 34 years were used. It was found that when the room temperature was raised to a dry-bulb reading of 95° F. or a wet-bulb reading of 85° F., there was a statistically definite fall in accuracy of wireless telegraphy reception compared with performance at a dry-bulb temperature of 85° F. or wet-bulb temperature of 75° F., or a dry-bulb temperature of 90° F. or 80° F. wet bulb. Since the velocity of the air was 100 feet per minute it was suggested that the effective temperatures of 79° F. to 83° F. were undoubtedly associated with a more effective wireless telegraphy reception than an effective temperature of 87.5° F. In the Eastern Fleet of the Royal Navy, wireless telegraphy ratings have to work at temperatures above 84° F. and even under more severe conditions. The exceptionally able men were less affected by harassing atmospheric conditions than those less efficient. The deterioration in performance as measured by the number of faulty wireless telegraphy messages bore a logarithmic relationship to the atmospheric temperature changes. This applied when the nature of the task was different, consisting simply of moving a heavy lever. There were no signs of phychological effects accumulating serially from day to day; in fact the men were usually better at the wireless

telegraphy test on the second day of a particular room temperature. The average number of wireless telegraphy errors per man per hour rose considerably and progressively within the third-hour watch period. Twice as many errors were made in the second hour and 3 or 4 times as many during the third hour.

Pezechkian (*1085*) 1949 measured the rates of work of rats running in a revolving drum exposed to temperatures ranging from 13° to 40° C. The rectal temperature did not vary much beyond normal range. The maximum capacity for work was noted in the 31° to 34° C. temperature range, particularly at 31° to 32° C. Beyond these temperatures the work decreased as much as 34 percent.

Mackworth (*1083*) 1948 administered performance tests to a group of sailors subjected to effective temperatures from 79° F. to 97° F. Results showed that there is a critical region of temperature above which most acclimatized men dressed in shorts will not work so accurately or sleep restfully. The region lies between effective temperatures of 83° F. and 87.5° F.; that is to say, between dry-bulb temperatures of 90° F. and 95° F. or wet-bulb temperatures between 80° F. and 85° F. The accuracy of very highly trained men was found to suffer to a less extent from the effects of high atmospheric temperatures than does the performance of men of ordinary ability. If a group of 12 to 20 men had been working at a sedentary task for 2 to 3 hours and if their average rectal temperature at the end of that time was found to be more than 100° F., then that group of men was not likely to have been working at full efficiency. This refers to acclimatized men dressed in shorts and cannot be used when the task entails heavy physical effort. There is no direct relationship between the rectal temperature and the incidence of mistakes. The association is noncasual, both rectal temperature and the error score being dependent upon the common factor of room temperature. These same conclusions have been reported by Mackworth (*1084*) in 1948. Mackworth (*1082*) 1946 has studied the effects of heat and high humidity on prolonged visual search as measured by a clock test. This test was devised to incorporate some of the main psychological features of a task in which the operator watches a radar tube. The task requires that the subject be sufficiently alert at all times to note faint and short-lasting visual signals, usually with no check on his working efficiency. During this test the optimum atmospheric temperature for accurate work was an effective temperature of 79° F. An increase in the effective temperature to 87.5° F. or a decrease to 70.0° F. produced an increase of 25 percent in the incidence of missed signals. Deterioration in the speed of work was not so striking as the decline in accuracy. At 97° F. effective temperature the responses became sluggish. Training appears to help to maintain accuracy in hot atmospheres. Mackworth reported that there is a rise in rectal temperature of the men doing this sedentary test, and he found a weakly positive association between the final rectal temperature and the incidence of missed signals during the second hour of the test. However, this relationship could not be statistically validated.

The performance of a motor coordination test by human subjects subjected to a hot, humid environment was shown to be impaired in studies of Weiner and Hutchinson (*1088*) 1945. Acclimatization of motor coordination, as revealed by the tests and analogous to acclimatization to work, appears to be suggested by these experiments; but if such an acclimatization to motor coordination does occur, the process must be different from acclimatization to work since the subjects already acclimatized in this respect gave an impaired coordination performance in the hot room. In a study of the performance of the pursuit-meter test under conditions of unfavorable atmospheric heat, Carpenter (*1075*) showed deterioration in work performance with high room temperature and with handle load. The results suggested that the effects of handle load are greater at increased room temperature, but this effect is unreliable statistically. Rectal temperatures taken at the end of the test and the amount of weight lost in sweat showed the expected relationship with room temperature, but the individual readings revealed no correlation with performance. Mental performance under heat stress as indicated by addition and number checking tests has been studied by Blockley and Lyman (*1072*) 1950. These experiments were conducted at a single humidity (vapor pressure of 0.8 in. of Hg) and at 3 levels of temperature: 160°, 200°, and 235° F. The duration of each exposure was determined by the ability of the individual to tolerate the heat. Work on the mental problems was continuous during the exposure, except for a 15-second rest period in each 3 minutes. No significant differences in performance were found for the 200° F. experiment, but in the two other experimental environments the performance in the final 6 minutes of heat exposure was found to be significantly poorer in the pre-exposure period. Cameron (*1073*) 1945 has made observations on the factors of stress operating on naval personnel based in India and Ceylon, and working under tropical conditions. His observations were based almost entirely upon the experiences

of the psychiatrist dealing with men who had suffered from breakdown. While a psychiatric survey must deal with the whole picture, an attempt was made to underline the elements particularly related to the effects of heat and humidity and to suggest possible lines of investigation. The first element of importance appeared to be that associated with "tropical loss of memory." This, the author considered, is largely a metabolic phenomenon and not primarily emotionally determined. The author also described a "prepsychotic tropical syndrome." This differs materially from the conditions that have been met with in men who experienced equal isolation and corresponding stress in nontropical overseas service. A high proportion of breakdowns in naval personnel on tropical service are stated to be psychotic in character. This is not the case according to the author in naval service in temperate climates, however arduous.

For further studies of the effects of heat on performance, papers by the following may be consulted: Carpenter (*1076*) 1949; G. Brit. MRC–R NPRC (*1078*) 1946; Henschel, Taylor, Brozek, Mickelsen, and Keys (*1079*) 1943; Lee (*1080*) 1949; Trenchard (*1086*) 1946; and U. S. NRC (*1087*) 1945.

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1073. Cameron, K. The psychiatric aspects of tropical service in the navy. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 45/252, H. S. 93,* December 1945, 7 pp. [P]

1074. Caplan, A. and J. K. Lindsay. An experimental investigation of the effects of high temperatures on the efficiency of workers in deep mines. Paper submitted for discussion at Meeting of Inst. Mining and Metallurgy, Oct. 17, 1946. Abstr: *Bull. Hyg., Lond.,* 1947, *22:* 333–334. [P]

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1081. Mackworth, N. H. Effects of heat on wireless telegraphy operators hearing and recording morse messages. *Brit. J. industr. Med.,* 1946, *3:* 143–158. *Bull. Hyg., Lond.,* 1946, *21:* 679–680. *R. N. P. 45/243, H. S. 88,* October 1945, 17 pp. *J. industr. Hyg.,* 1947, *29:* abstract section: 3 [P]

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1085. Pezechkian, M. Influence de la température extérieure sur la capacité de travail musculaire chez le rat. *C. R. Soc. Biol., Paris,* 1949, *143:* 242–244. [P]

1086. Trenchard, H. J. Inability to work in a tropical climate. *Brit. med. J.,* 1946, *2:* 416–418.

1087. U. S. NRC. Subcommittee on clothing. Conference on "working efficiency and high temperatures". 23 October 1945, 15 pp.

1088. Weiner, J. S. and J. C. D. Hutchinson. Hot humid environment: its effect on the performance of a motor co-ordination test. *Brit. J. industr. Med.,* 1945, *2:* 154–157. [P]

F. HEAT DISEASE

For general studies of heat disease, papers by the following should be consulted: Borden, Waddill, and Grier (*1089*) 1945; Conn (*1091*) 1940; Napier (*1102*) 1946; Reed and Harcourt (*1103*) 1941; Shattuck (*1106*) 1951; Talbott (*1107*) 1950; and Talbott, Dill, Edwards, Stumme, and Consolazio (*1108*) 1937. These authors divide heat disease into the following categories: (1) heat collapse or heat prostration, (2) heat exhaustion, (3) heat stroke, and (4) heat cramps. In heat prostration there is evidence of peripheral vascular collapse with poor venous return. There may be no rise in body temperature, and the symptoms are mainly those of hemodynamic failure. The patient may be anxious, the skin cold and clammy, the pupils dilated, and the blood pressure below normal. The condition is usually reversible. There is decrease of chloride in the urine, and in some cases a fall in the hemoglobin concentration. Such patients usually

are not in collapse long enough to require intravenous administration of saline or whole blood, and administration of water and salt by mouth is considered adequate therapy ordinarily. Heat exhaustion is characterized by weakness, lassitude, headache, dizziness, vomiting, mild cramps, sleeplessness, rapid pulse, low blood pressure, and slight fever. The urinary chloride is low or absent. There may be fainting at work and psychological symptoms. Peripheral vascular insufficiency is characteristic and the condition is described as akin to Addisonian crisis with diminution of extracellular fluid and sodum chloride reserve. There may be hemoconcentraton with elevated red and white blood counts. Treatment consists in removal of the patient from the surroundings causing the condition, regulation of diet and fluid intake, and replacement of fluid and salt.

For reports on heat stroke, papers by the following should be consulted: Kirk (*1097*) 1946; Krainer (*1098*) 1949; Logue and Hanson (*1099*) 1946; Malamud, Haymaker, and Custer (*1101*) 1946; Schickele (*1105*) 1947; Waterlow (*1109*) 1947; and Wright, Repport, and Cuttino (*1111*) 1946. In heat stroke there is rise of body temperature and symptoms related to organic changes, especially in the nervous system. Krainer (*1098*) 1949 has drawn attention to severe degeneration of Purkinje cells with a picture of atrophy of the cerebellum in a case of fatal heat stroke with hyperpyrexia. This patient described by Krainer survived the hyperpyrexial attack for 19 days in a state of unconsciousness and coma. Logue and Hanson (*1099*) 1946 have reported jaundice believed to be due to the toxic effect of the hyperpyrexia. The electrocardiographic changes are noted as confusing and similar to those of pericarditis, but without an elevation of the ST-segment. The report of Malamud, Haymaker, and Custer (*1101*) 1946 is based on a study of 125 fatal cases of heat stroke which occurred in the U.S. Army during the summer months of 1941 to 1944 in military installations in the Southern States. Soldiers were undergoing strenuous muscular exercise at high environmental temperatures. Lack of sufficient acclimatization seems to have been a predisposing factor. The clinical data established three categories of signs and symptoms: (1) those due primarily to hyperthermia, namely, manifestations of the central nervous system, (2) those due secondarily to shock, and (3) those due to complications, such as bronchopneumonia, and lower nephron nephrosis arising during the illness. Some cases were of acute onset with early persistent coma or delirium. In other cases coma was the presenting symptom at the onset with remission or late relapse. In some cases the onset was insidious with a progressive course and late development of coma. The duration of the disorder varied from less than an hour to 12 days. In 30 percent of the cases the illness lasted more than 24 hours. In the authors' cases the most frequent laboratory findings were early development of leukocytosis, hemoconcentration, rise in the nonprotein nitrogen, and a decrease in the carbon dioxide combining power. Pathological changes in the central nervous system consisted of progressive degeneration of neurons with gliosis in the cerebellum, cerebral cortex, and basal ganglia, but not in the hypothalamus. There were also congestion, edema, and petechial hemorrhages. The hemorrhages occurred in a wide variety of structures, regardless of the duration of the illness, and were seen especially in the lungs. According to the authors the clinical, laboratory, and pathological findings indicate two factors operative in heat stroke—hyperthermia and shock. It would seem that increased body temperature imparts to the disorder a specific character, affecting body tissues to varying degrees. The hypothesis is advanced that heat irreparably damages the thermostatic function of the hypothalmus and that as a consequence the autonomic nervous system is no longer capable of reestablishing sweating or adequate peripheral circulation. Where anoxic anoxia or other conditions are combined with severe shock, the same sequence of clinical events may follow. The authors believed that although shock plays a significant part in heat stroke it is a secondary event and nonspecific. Purpuric manifestations of heat stroke have been described by Wright, Repport, and Cuttino (*1111*) 1946. Determinations of prothrombin time and platelet counts were made on 12 patients critically ill with heat stroke. It was concluded that the hemorrhagic phenomena associated with heat stroke are due to increase in capillary porosity and decrease in prothrombin and/or platelets. The prothrombin deficiency was thought to be secondary to hepatic damage. Early transfusions of whole blood and means to prevent or retard damage to the liver were considered as possibly of value in treating those patients who survive the first few hours.

Although the pathogenesis of heat cramps is to some extent puzzling, it appears certain that the condition is due to excessive perspiration and restoration of fluids by drinking pure water so that chlorides lost in perspiration are not replaced. Heavy physical exertion in a hot environment is the predisposing factor. Heat is more important than humidity, and the condition is less likely to occur in environmental temperatures below 100° F. than those above. Vomiting is a further predis-

posing factor since there may be additional loss in this way of chloride in the gastric contents. The skin may be pale and wet with perspiration, but signs or symptoms of shock are not usually present. The mortality rate is negligible. The principal symptom consists of muscle spasms in which the muscles may contract to a state of boardlike rigidity with agonizing pain. The cramps usually occur in muscles which are most used and may commence during or after work. The muscles of the fingers, forearms, arms, legs, pelvic girdle, and abdomen may be particularly affected. The involuntary muscles are spared. When the contraction passes, the pain is immediately relieved, but the muscles remain tender. The spasms may be reinitiated by active movements, trauma, or cold drafts on the body. There may be only a slight diminution in urinary output, but there is a decreased concentration of sodium and chloride in the serum and in the urine. In fact, chloride may be entirely absent in the urine. Plasma protein, potassium, phosphorus, and calcium are increased, and there may be some hemoconcentration with increase in the red blood count. The cramps are relieved by replacement of sodium and chloride as well as fluids. However, the replacement of fluids is considered of secondary importance. Relief of symptoms by sodium and chloride supports the hypothesis that the etiology of heat cramps relates to body depletion of essential electrolytes. Treatment consists of copious saline drinks of intravenous or rectal administration of saline solution if necessary. Morphine has been recommended for cramps, but some authors consider that morphine in therapeutic doses in severe cramps is not effective. Prevention of heat cramps may be successfully attained by administration of water containing salt tablets, from 10 to 30 grains of sodium chloride to each pint of water. Fleischmann (*1095*) 1947 has reported relief of pain in cramps from excessive water loss by active movement of antagonists of cramped muscles or passive movement of the limb in the direction opposed to that of the contracted muscle's action.

For further reports on heat disease, papers by the following may be referred to: Brown (*1090*) 1947; Consolazio, Pecora, and Tusing (*1092*) 1947; Daily and Harrison (*1093*) 1948; Fergusson (*1094*) 1948; Heilbrunn, Harris, Le Fevre, Wilson, and Woodward (*1096*) 1946; McCarthy (*1100*) 1943; Rosenbaum (*1104*) 1946; and Weaver (*1110*) 1948.

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1101. Malamud, N., W. Haymaker, and R. P. Custer. Heat stroke. *Milit. Surg.*, 1946, *99:* 397–449. [CH]

1102. Napier, L. E. Diseases due to the direct effects of a tropical climate. pp. 34–51 in: *The principles and practices of tropical medicine.* New York, The Macmillan Company, 1946, 917 pp.

1103. Reed, J. V. and A. K. Harcourt. Abnormalities of temperature. Excessive degrees of heat causing general disturbances. pp. 101–106 in: *The essentials of occupational diseases.* Springfield, Charles C. Thomas, 1941, 225 pp.

1104. Rosenbaum, L. Significance of salt (NaCl) in torrid temperatures. *Milit. Surg.*, 1946, *98:* 43–47. [P]

1105. Schickele, E. Environment and fatal heat stroke. An analysis of 157 cases occurring in the army in the U. S. during World War II. *Milit. Surg.*, 1947, *100:* 235–256.

1106. Shattuck, G. C. Acute effects of heat. pp. 729–740 in: *Diseases of the tropics.* New York, Appleton-Century-Crofts, Inc., 1951, 803 pp. [R]

1107. Tolbott, J. H. Heat: pathologic effects. pp. 406–409 in: *Medical physics. Volume II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

1108. Talbott, J. H., D. B. Dill, H. T. Edwards, E. H. Stumme, and W. V. Consolazio. The ill effects of heat upon workmen. *J. industr. Hyg.*, 1937, *19:* 258–274.

1109. Waterlow, J. C. Heat-stroke and heat-exhaustion in Iraq. *Brit. med. Bull.*, 1947, *5:* 3–4.

1110. Weaver, W. L. The prevention of heat prostration by use of vitamin C. *Sth. med. J., Birmingham,* 1948, *41:* 479–481. *J. industr. Hyg.*, 1949, *31:* abstract section; 69–70. [P]

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G. SKIN DISEASES ASSOCIATED WITH HEAT AND HUMIDITY

A number of affections of the skin may provide a hazard under conditions of military operations in hot climates or submarine action in tropical waters without adequate air conditioning and ventilation. For a consideration of common skin diseases of the tropics, a report by Napier (*1120*) 1946 should be consulted. Probably the most important and widespread of these skin conditions is prickly heat or heat rash, formally designated *miliaria rubra.* Prickly heat occurs in all tropical and many subtropical countries, especially during periods of high humidity. It is stated to be more common in newly arrived white men, and is more severe in infants and children than in adults. It is more common in men than in women and in thick-set individuals than in spare, thin persons. It appears to occur more usually in blond, fair-skinned people than in those with darker complexions and is more pronounced in obese subjects. Failure to bathe or change the clothes regularly may predispose towards prickly heat. The condition occurs on parts of the body where clothes are held in close contact by pressure, particularly around the waist and shoulders. Friction from clothes, especially in the groin, axilla, and backs of the wrists, may aggravate the condition. It occurs commonly in those areas where two skin surfaces are in continuous contact, as between folds of fat. The lesion consists of red papules and minute clear vesicles with a surrounding red halo. The skin has a red granular appearance with a rough texture. Later there may be a white powdery desquamation. Factors causing hyperemia of the skin, such as exercise or a hot bath, may result in an immediate exacerbation of the pricking sensation and the intolerable itching which is characteristic. The symptoms may be so insistent as to dominate the attention of the sufferer and interfere with sleep and performance of duty. From a series of clinical observations on a large group of naval officers, Fay and Susman (*1115*) 1945 concluded that the following factors increase liability to prickly heat: (1) age over 30, (2) fair skin, (3) highly strung emotional makeup, (4) large salt intake, (5) working and sleeping below decks, (6) high temperatures in the work place, (7) long working hours, and (8) battle dress or poorly ventilated clothing. It was stated by the authors that personnel belonging to group O may have a greater predisposition to heat rash than those in other blood groups. The following factors were said to reduce liability: (1) age below 30, (2) previous suntan, (3) loose clothing, (4) working and sleeping in open air, (5) low temperature of the work place and, as a possible factor, (6) membership in blood group A. The following factors were listed as not affecting incidence: (1) weight, (2) sweat reaction, (3) open-neck shirts, and (4) effects of sun on the skin. Inconclusive factors listed included type of work, humidity, and brands of soap used.

Sulzberger and Emik (*1134*) 1946 reported that 66 percent of personnel of a research group on Guam suffered from prickly heat. These authors also indicated that the incidence of the condition was greater in blond, fair-skinned people or in red-headed persons than in others. They likewise reported no difference in incidence between over- and under-weight persons. Those who were working in particularly hot, humid spaces, as in the laundries or the kitchens, had no higher incidence than other members of the group, but the eruptions in the group working in the laundries and kitchens were longer lasting and more disagreeable. Work for 8 hours in an air-conditioned environment during a 24-hour day reduced the incidence. Prickly heat was found not to be related to race or former habitat. Sulzberger and Zimmerman (*1135*) 1946 observed that patches of prickly heat exhibited a reduction or absence of sweating as compared with normal areas of skin. Horny plugs were seen in the sweat-duct orifices, and edema was found around the ducts in the epidermis and upper corium. There was also periductal cellular infiltration. The acini of the sweat glands were found to be morphologically altered. These authors advanced the hypothesis that profuse sweating leads to maceration of the skin's surface, faulty keratinization, occlusion of the sweat pores by horny plugs, and irritation of the tissues by substances derived from concentrated or retained sweat in the orifices and superficial portions of the ducts. This chain of events was believed to constitute the pathological process in the production of prickly heat.

An experimental study of heat rash in volunteer subjects has been reported by Duffner (*1114*) 1946. Subjects carried out work 7 hours a day at a dry-bulb temperature of 108° F. (83° F. wet bulb, effective temperature 90° F.). They spent the remaining 17 hours of the day in another room at a dry-bulb temperature of 95° F. (83° F. wet bulb, effective temperature 87° F.). Work consisted of walking on a treadmill. A similar group worked 7 hours a day in the hot treadmill room, but spent

the remaining 17 hours in a temperature of 85° F. dry bulb (71° F. wet bulb, effective temperature 78° F.). Each group carried out the program for 10 days. All of the subjects in the "hot group" developed heat rash, covering an average of 39 percent of the skin surface. One-half of these men complained that they were unable to sleep due to discomfort. Only one man in the "cool group" developed heat rash, and in this case only 15 percent of the body surface was involved. In a further experimental series a "hot group" spent 3 hours a day in the hot treadmill room and the remaining 21 hours in hot quarters. A "cool group" spent 3 hours a day in the hot treadmill room, 9 hours a day in hot quarters, and 12 hours in cool quarters. These conditions were maintained for 30 days. Eleven out of 18 of the "hot group" developed heat rash as early as the third day in the hot atmosphere, with maximum severity on the 9th to 13th day. The "cool group" did not have heat rash. The author concluded that spending as little as 12 hours a day in an atmosphere in which one does not sweat at rest will prevent the occurrence of heat rash. Blum, Gersh, and Spealman (*1113*) 1945 have reported that heat rash is a rapidly reversible condition, at least during the first week of exposure to hot environments. In these studies, exposure to ultraviolet radiation before entering the hot environment inhibited the development of heat rash in all 5 subjects of 1 experiment, but not in any of 6 subjects in another, a discrepancy not easily explained. Cold baths appear to have a slight ameliorating effect on the rash. Neither pressure nor friction, nor the inhibition of sweating by formalin, prevented the development of heat rash. Increase in white blood cell counts with relative lymphocytosis was observed in all 6 participants in 1 experiment in which blood counts were made. Change in pH of the sweat was not found to be associated with heat rash. There was no change in elasticity of the skin, in the rate of histamine wheal formations, or saline wheal disappearance in association with heat rash.

Shelley and associates have reported a series of studies in which heat rash has been produced experimentally in man. In the first report of this series, Shelley, Horvath, Weidman, and Pillsbury (*1131*) 1948 brought about local anhidrosis and sweat retention vesicles by a single treatment of the skin with iontophoresis. It appeared that a minor superficial epidermal injury was produced, not directly affecting the acini of the sweat gland, with a resultant hyperkeratosis which led to a transitory sweat-duct obstruction. This resulted in local sweat retention anhidrosis and vesicles containing sweat. Various kinds of experimental stimulation were found by Shelley, Horvath, Weidman, and Pillsbury (*1130*) 1948 to be effective in the production of experimental heat rash in human subjects. These were: (1) iontophoresis, (2) ultraviolet light, (3) heat, (4) carbon dioxide ice, (5) maceration, (6) adhesive tape, (7) aluminum chloride, (8) soap, (9) phenol, and (10) chloroform. No immediate alteration was noted in the normal sweating processes when the subjects were stimulated to vigorous sweating by means of heat. However, within 3 to 5 days definite changes were observed within the areas of the skin treated. They varied from slight to striking anhidrosis; in the areas of greatest anhidrosis, small, clear, superficial vesicles developed. These vesicles did not appear in areas in which the secretion of sweat was locally inhibited by atropine. These phenomena could be demonstrated repeatedly over a period of 1 to 2 weeks, after which the sweat function returned to normal. Microscopic studies revealed tiny plaques of hyperkeratosis in the treated areas. The vesicles were found to be situated entirely within the stratum corneum, and serial sections demonstrated that they were directly connected with the sweat ducts. It was concluded by the authors that the factor common to all stimuli applied was that of minor irritation, and the plugging of the sweat-gland orifices. These studies have also been reported by Shelley and Horvath (*1127*) 1950. In a further report Shelley and Horvath (*1128*) 1950 indicated that three separate factors are essential in the pathogenesis of experimental heat rash: (1) a minor epidermal injury, (2) intensive sweating for several hours, and (3) individual susceptibility. Alone, none of these factors was found to be sufficient. In a susceptible subject, hyperkeratotic plugging of the sweat duct results in sweat retention following which a single heat exposure of several hours leads to disorganization of the upper end of the sweat duct due to pressure of the entrapped sweat. Shelley (*1126*) 1951 distinguished four distinct types of sweat retention which could be experimentally identified: (1) collection of sweat in a papulovesicle in the stratum corneum, (2) collection of sweat in an intramidepidermal papulovesicle, (3) collection of sweat in a dermal papulovesicle just beneath the epidermis, and (4) simple retention of sweat within the dermis without any clinical signs or symptoms.

Sulzberger, Zimmerman, and Emerson (*1136*) 1946 have inferred that ordinary prickly heat and tropical anhidrotic asthenia are different manifestations of the same fundamental process. Distention

and changes of pressure due to secretion of sweat into the plugged ducts contribute to the sensory disturbances in prickly heat, and these symptoms vanish in tropical anhidrosis following the relief of tension through rupture or other kinds of damage of the ducts and free drainage of sweat into the surrounding area. O'Brien (*1121*) 1947 has advanced the suggestion that heat rash is a manifestation of sebaceous deficiency of the skin, mainly the result of the many lipoid-depriving influences that act upon the skin from without. The stratum corneum, when deficient in lipoid, becomes the obstructing agent plugging the sweat gland. The value of keratolytic substances in removing the keratin plugs produced in heat rash is stressed. The author recommended a routine of skin hygiene in the tropics designed to reduce lipoid deprivation of the skin to a minimum. In a discussion of tropical anhidrotic asthenia, O'Brien (*1122*) 1948 pointed out that miliaria (heat rash) is distinguished by malaise, distaste for work, excessive fatigue, and loss of acclimatization. Particularly there are asthenic symptoms, exhaustion, headache, dyspnea, and giddiness when working in the heat. Also, after exercise there may be gross cardiorespiratory distress and an anhidrosis on the covered areas of the body. The body temperature does not rise as high as could be expected. The author postulated that the symptoms result from circulatory failure of a peripheral type. Miliaria predisposes toward hyperpyrexia. By causing an increase in the sodium chloride concentration in the sweat miliaria may predispose toward heat exhaustion. Ladell (*1118*) 1951 found that an otherwise healthy subject on recovery from miliaria exhibited a diminished tolerance to heat and an increased rate of sodium chloride loss in the sweat, compared with figures on the same subject obtained before prickly heat had developed.

Heat rash is easier to prevent than to cure. Under conditions of combat operations in the tropics it may be a cause of many lost man-days as well as a source of great annoyance and discomfort. It also imposes a heavy burden upon the medical department at an inopportune time. As Ribble, Luedemann, and Peabody (*1124*) 1947 have stated, the most effective means of preventing heat rash is the provision of a suitable environmental temperature. Air conditioning in the submarine will eradicate the condition. Reassignment of bunks should be effected when possible to enable men working in hot places or performing heavy physical work to sleep in the coolest part of the vessel. Auxiliary precautions consist of the judicious use of electric fans, avoidance of very hot baths, frequent changes of underwear and other clothing, and avoidance of local overtreatment. It should be stressed that adequate air conditioning, in addition to its many other values, is effective prophylaxis against this condition which is so costly in its lowering of morale and overall efficiency of the crew. For further studies on treatment of heat rash the following references may be consulted: (*1117, 1123,* and *1137*). Attention may be particularly directed to a statement by Horne and Mole (*1117*) 1950 that prickly heat is relieved by increasing fluid intake and by reducing salt intake. It can be made to relapse by increasing the intake of table salt. Radclyffe (*1123*) 1947 has recommended the use of benadryl to alleviate, but not cure, prickly heat. Within a period of several hours after taking 100 mg. of benadryl there is a blanching of the affected area and relief from itching. After 1 or 2 days of taking benadryl there is stated to be a complete remission of symptoms.

For a description of athlete's foot (trichophytosis, epidermophytosis, Hong Kong foot, tinea pedis) an article by Napier previously referred to (*1120*) should be consulted. This condition is more widespread and serious in humid tropical environments and under conditions of naval operations on hot decks. The etiological organism is a fungus usually of the Trichophyton species. It may also be caused by Epidermophyton floccosum and by Candida albicans. The organisms penetrate the epidermis and the primary site is usually between the fourth and fifth toes. The condition spreads to other interdigital spaces and to the soles of the feet, the dorsum and other sites on the feet, ankles, and nail beds. There are small vesicles surrounded by a halo of inflammation. Pieces of sodden epithelium separate, exposing the red corium. There may be bleeding as a result of scratching and the lesions may become infected with pyogenic micro-organisms. There may be areas of hyperkeratosis at the margins of the lesions. Serious cellulitis is a potential hazard. Prevention consists in avoiding infection by using washable slippers in shower quarters, by not going barefoot on wet floors, and not using towels and slippers in common. Changing the socks twice daily and washing the socks thoroughly may be helpful in reducing the seriousness of the condition. Hygiene of the feet is important; after washing they should be carefully dried and may be dusted with antiseptic powder. Several preparations for local application have been recommended, but it should be pointed out that the greatest danger is overtreatment. It is perhaps best to be content to keep the conditions inactive.

Furunculosis may be present in submarine personnel under conditions of operation. Reference is

made to reports by the following: Barnes (*1112*) 1943; Gant, Owens, and Schwartz (*1116*) 1942; Liles (*1119*) 1947; and Sukhtankar (*1132*) 1949. The paper by Gant, Owens, and Schwartz (*1116*) 1942 discusses an epidemic of boils in a group of tunnel workers. This investigation reveals that the outbreak of boils was related to a combination of factors bringing about a lowering of skin resistance to bacteria. The causes of the outbreak were related to the humid atmosphere, perspiration, warm tunnel water, friction from clothes and rubber coats infiltrated with rock dust, together with the unhygienic conditions of the tunnel, and the unsanitary and dirty state of the working clothes.

According to Sulzberger, Addenbrooke, Joyce, Greenberg, and Mack (*1133*) 1946, a varient of *acne vulgaris* had a high incidence and was a great cause of discomfort and loss of effectiveness among military personnel in the tropics. This form of acne differed from adolescent acne vulgaris in several significant respects, particularly age of onset, localization, and course. It was found to be brought on or made worse by heat and high humidity, and tended to improve when the patients are removed to a cool, dry environment. Occlusion of the ducts of hyperactive sebaceous glands seems to be the essential pathological process.

For further reports on skin diseases associated with heat and humidity, the following are listed: Robertson (*1125*) 1945, and Shelley, Horvath, and Pillsbury (*1129*) 1950.

1112. Barnes, B. Furunculosis-etiology and treatment. *J. clin. Endocr.*, 1943, *3:* 243–244. [CH]

1113. Blum, H., F. I. Gersh, and C. R. Spealman. Studies of experimental heat rash, U. S. NMRI. *Project X–479, Rept. no. 1,* 27 December 1945, 10 pp. [P]

1114. Duffner, G. J. Heat rash as a problem in the naval service. *Amer. J. trop. Med.*, 1946, *26:* 539–541.

1115. Fay, F. R. and E. Susman. On the prickly heat. *Med. J. Aust.*, 1945, *2:* 453–456.

1116. Gant, J. W., R. J. Owens, and L. Schwartz. An epidemic of boils in a group of tunnel workers *Publ. Hlth. Rep., Wash.*, 1942, *57:* 612–617.

1117. Horne, G. O. and R. H. Mole. The effect of water and salt intake on prickly heat. *Lancet, Lond.*, 1949, *2:* 279–281. *Abstr. World Med.*, 1950, *7:* 295. [P]

1118. Ladell, W. S. S. Changes in sweating after prickly heat. *Brit. med. J.*, 1951, *1:* 1358–1360. [CH]

1119. Liles, J. H. The local treatment of furuncluosis with penicillin. *U. S. nav. med. Bull.*, 1947, *47:* 645–650. [CH]

1120. Napier, L. E. Some common skin diseases of the tropics. pp. 570–585 in: *The principles and practice of tropical medicine.* New York, The Macmillan Co., 1946, 917 pp.

1121. O'Brien, J. P. A study of miliaria rubra, tropical anhidrosis and anhidrotic asthenia. *Brit. J. Derm. Syph.*, 1947, *59:* 125–158.

1122. O'Brien, J. P. Tropical anhidrotic asthenia. *Arch. intern. Med.*, 1948, *81:* 799–831. [R] [D]

1123. Radclyffe, L. Alleviation of prickly heat. *Brit. Med. J.*, 1947, *2:* 1012. [D]

1124. Ribble, G. B., W. S. Luedemann, and S. M. Peabody. Epidemic of prickly heat on aircraft carrier. *Nav. med. Bull., Wash.*, 1947, *47:* 77–82.

1125. Robertson, A. M. Prickly heat and tropical pemphigus. *J. R. nav. med. Serv.*, 1945, *31:* 258–260.

1126. Shelley, W. B. Experimental miliaria in man. IV. Sweat retention vesicles following destruction of terminal sweat duct. *J. invest. Derm.*, 1951, *16:* 53–64.

1127. Shelley, W. B. and P. N. Horvath. Experimental miliaria in man. II. Production of sweat retention anidrosis and miliaria crystallina by various kinds of injury. *J. invest. Derm.*, 1950, *14:* 9–20.

1128. Shelley, W. B. and P. N. Horvath. Experimental miliaria in man. III. Production of miliaria rubra (prickly heat). *J. invest. Derm.*, 1950, *14:* 193–204.

1129. Shelley, W. B., P. N. Horvath, and D. M. Pillsbury. Anhidrosis; An etiologic interpretation. *Medicine, Baltimore*, 1950, *29:* 195–224.

1130. Shelley, W. B., P. N. Horvath, F. D. Weidman, and D. M. Pillsbury. Experimental miliaria in man. I. Production of sweet retention anidrosis and vesicles by means of iontophoresis. *J. invest. Derm.*, 1948, *11:* 275–291.

1131. Shelley, W. B., P. N. Horvath, F. D. Weidman, and D. M. Pillsbury. Experimental miliaria in man. II. Production of sweat retention anidrosis and vesicles by various kinds of injury. *Amer. J. Physiol*, 1948, *155:* 469.

1132. Sukhtankar, K. M. A new treatment of furunculosis with whole liver extract. *J. Indian med. Ass.*, 1949, *18:* 245–246.

1133. Suzberger, M. B., E. F. Addenbrooke, S. J. Joyce, S. Greenberg, and A. G. Mack. Tropical acne. *Nav. med. Bull., Wash.*, 1946, *46:* 1178–1184.

1134. Sulzberger, M. B. and L. O. Emik. Studies on prickly heat. I. Clinical and statistical findings. *J. invest. Derm.*, 1946, *7:* 53–60.

1135. Sulzberger, M. B. and H. M. Zimmerman. Studies on prickly heat. II. Experimental and histologic findings. *J. invest. Derm.*, 1946, *7:* 61–68.

1136. Sulzberger, M. B., H. M. Zimmerman, and K. Emerson. Tropical anidrotic asthenia (thermogenic anhidrosis) and its relationship to prickly heat. *J. invest. Derm.*, 1946, *7:* 153–164.

1137. U. S. Navy, Technical mission to Japan. Heat rash and fungus infection. p. 43 in: *Aero, surface, and submarine medicine and research in the Japanese navy. Fascile M–1, Terget M–06,* 4 September 1945, 72 pp.

1138. Anon. Prickly heat and tropical asthenia. *Brit. Med. J.*, 1947, *2:* 779. [D]

VI. COLD EXPOSURE PROBLEMS

A. GENERAL CONSIDERATIONS OF COLD

In the compilation of references on cold exposure problems, the usefulness of these references as source material for the section on clothing (p. 284) has been kept in mind. In submarine operations, the cold problems are somewhat different from those encountered in surface ships in that conditions of

dampness as well as cold may prevail. Heating of surface vessels presents less of a problem, but the special conditions of submerged operations of submarines may make it difficult to adequately heat submarine compartments operating in Arctic waters. When the submarine is submerged, the only source of power is the batteries, and this power must be conserved for propulsion and other important engineering functions. Snorkel operations and use of atomic power modify the heating situation. Submarine crews encountered cold and wet weather on the deck, and cold exposure problems also come into the picture in connection with submarine rescue of survivors at sea. The following have prepared general reports which will serve to introduce the reader to the subject of physiological and pathological effects of cold: Brobeck (*1141*) 1946; Josiah Mach, Jr., Foundation (*1145a*) 1952; Talbott (*1149*) 1940; and Weiner (*1150*) 1949.

1139. Benitte, A. C. La guerre et le froid. Étude sur le comportement de l'homme aux basses températures. Ministère de la Guerre. Du Bulletin d'Information Technique et Scientifique. *N 21/G et N 22G,* 1948. [D]

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1141. Brobeck, J. R. Physiology of heat and cold. *Annu. Rev. Physiol.,* 1946, *8:* 65–88. [R]

1142. Gt. Brit. MRC—RNPRC, HS. Military requirements for research into the effects of cold climates on man. *R. N. P. 48/424, H. S. 223,* January 1948, 3 pp.

1143. Gt. Brit. MRC–RNPRC, HS. Memorandum on research problems into effects of cold environment. *R. N. P. 48/423, H. S. 222,* 10 June 1948, 4 pp.

1144. Johnson, R. E., and C. G. Bly. Metabolic changes in heat acclimatized men during abrupt exposure to a very cold climate. *J. clin. Invest.,* 1949, *28:* 792. Abstr.

1145. McCollum, E. L. Survey of human adjustment problems in the northern latitudes. Morale survey of Alaskan air command. USAF. Ladd air force base, Alaska. Arctic aeromedical laboratory. *Project 21–01–022, Program C, part 1–C,* 1 August 1950, 12 pp. [P]

1146. Metz, B. L'homme et le froid. *Strasbourg-méd.,* 1950, *1:* 303–321. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 758. [R]

1147. Park, R. G. Disorders due to cold. *J. industr. Hyg.,* 1946, *28:* abstract section: 28.

1148. Pugh, L. G. C. Physiological studies in H. M. S. *Vengeance:* Royal Navy cold weather cruise, 1949. Gt. Brit. MRC–RNPRC, CES. *R. N. P. 49/561, C. E. S. 306,* September 1949, 44 pp. [P]

1149. Talbott, J. H. The effect of cold. pp. 664 (20–1)—664 (20–45) in: *Oxford medicine,* Vol. IV, Part III. Edited by H. A. Christian. New York, Oxford University Press, 1940. [R]

1150. Weiner, J. S. Progress report on Arctic cruise 1949. Gt. Brit. MRC–RNPRC, CES. *R. N. P. 49/508, C. E. S. 281,* 1 February 1949, 5 pp.

B. PHYSIOLOGICAL EFFECTS OF COLD

For general studies on the physiological effects of cold, the reader is referred to papers by Nei and Tada (*1197*) 1950; Pugh (*1199*) 1950; Radsma (*1200*) 1950; and U. S. NRC (*1215*) 1943. In Radsma's studies, normal human subjects remained for a whole morning either in an ordinary tropical room with an average dry-bulb temperature of 29° C. and a relative humidity of 70 percent, or in a cool room with a dry-bulb temperature of 22 to 24° C. and a relative humidity of 65 to 70 percent. It was found that the metabolic rate was depressed in the cool room and that body temperature fell. Under conditions of cold there was an increase in the volume of urine excreted with increased excretion of sodium and chloride. The pulse rate was higher in the warm room, but there were only slight changes in arterial blood pressure, oxygen saturation of the blood, and minute volume of circulation. In the cool room there was at first a slight increase in respiratory rate and alveolar carbon dioxide tension, but no significant difference in the pH of the blood or urine.

Numbness and pain in the extremities constitute a complicating hazard of cold. In a report of experiments carried out on 40 subjects at Fort Churchill, Mackworth (*1189*) has stated that there was much greater numbness in the subjects at temperatures between −30° and −35° C. than at −25° to −30° C. At these temperatures a wind velocity of greater than 6 miles an hour increased the loss of tactile discrimination and enhanced the numbing of the fingers. In 1949, Kunkle (*1188*) reported a study of phasic pains induced in 24 adult subjects by cold. One hundred and fifty experiments were performed in which the digit of one hand was immersed in a large crock of ice water maintained at 0° C. Immersion continued from 20 minutes to 2 hours. Reports of pain intensity were given by the subjects at 20-second intervals. After 10 to 60 seconds, an aching pain was reported in the digit, rising to a peak by the end of second to fourth minute. Superficial anesthesia and analgesia was observed by the end of the fourth to seventh minutes and at about the tenth minute, the finger felt numb. Following this, sensibility returned with a second pain peak which then slowly subsided until the fifteenth to twentieth minute, all pain was gone. Following removal of the digit from the ice water, there was pain for approximately 2 minutes. Some subjects developed a brief presyncopal reaction with giddiness, sweating, facial pallor, and bradycardia after the second pain peak. The author associates the first pain peak with cold and vasoconstriction. This first

pain peak is attributed to direct injury of chilled tissues or nerves and may be mediated by a metabolite locally released. The second pain is believed to be associated with reactive vasodilatation and consequent warming with return of function in sensory nerves earlier paralyzed by cold. These phenomena are relevant to the unusual susceptibility to cold pain commonly observed in the digits of patients with Raynaud's disease and in injured tissues with impairment of local circulation and deep hyperalgesia.

Blaisdell (*1160*) 1951 has reported variations in pain and temperature sensation accompanying cold-induced cyclic vasodilatation in fingers exposed to cold air of 0°, 5°, and 10° C. In these experiments, the initially appearing sensations of increasing cold and pain were spontaneously relieved by sensations of relative warmth and complete abatement of pain with the occurrence of each vasodilatation wave. These profound sensory changes occurred not only when the body as a whole was warm but also when it was cold. In certain unpredictable instances, spontaneous rewarming of the finger during a vasodilatation wave proceeded to a complete loss of sensation in air temperatures of 0° and 5° C. Three types of pain related to cold were observed: (1) "First pain," a dull pain of increasing severity occurring during objective and subjective cooling; (2) "Second pain," a burning and throbbing pain observed in a few instances, occurring only after a preceding numbness due to severe cooling during early spontaneous rewarming while the finger remained exposed to cold; and (3) "Afterpain," also burning and throbbing in character and experienced upon removal of the finger from the cold, and also after the numbness of frostbite during exogenous rewarming. This latter pain was relieved by circulatory arrest but returned with the restoration of blood flow. Blaisdell considered that the "first pain" is due to the direct affect of cold upon neural sensory mechanisms. "Second pain" was believed to result from the return of function to nerves paralyzed by cold and to reactive vasodilatation. "Afterpain" seemed mainly a consequence of the reactive vasodilatation of exogenous rewarming. It was suggested that steep, spatial, thermal gradients established by warm blood entering the cool finger may contribute to "second pain" and "afterpain."

In environmentally produced hypothermia of the unanesthetized rat, mouse, or kitten, there occurs a progressive descending paralysis of the central nervous system. Hamilton (*1179*) 1937 has reported in these animals the abolition of higher nervous functions, locomotion, voluntary movements, attitudes, equilibration, hearing, and vision. Following this, swallowing, biting, and corneal and flexor reflexes are abolished. Finally, the medullary centers are affected with resultant respiratory failure and death. The responses which are the last to disappear are the first to recover. The manner of central nervous system involvement nad recovery indicates to the author the narcotizing nature of hypothermia. Even at body temperatures below 70° F. the homeothermic animal attempts to resume a normal level of body heat. In body temperatures so low that nervous reactions and other evidences of life may be indiscernible, the animal can remain alive and subsequently recover.

The effects of exposure of human subjects to ambient temperatures from −50° to +117° F. upon reaction time have been reported by Coakley, Forlano, and Barmack (*1164*) 1948. The performance measured was simple discrimination and choice reaction time. Performance was found not to vary significantly with low ambient temperatures, provided that the body generally and the responding member in particular was properly protected. During exposures for several days to temperatures as low as −20° F., clothing was found adequately to protect the body without interfering significantly with the speed of simple reaction. For periods of about an hour, current-type clothing provides adequate protection against ambient temperatures as low as −50° F. Conditions which reduce strength and dexterity of movement were found to leave reaction time unchanged. Moreover, the reaction time did not vary significantly with high ambient temperatures up to +117° F., provided the wet-bulb temperature did not exceed about 86° F. Some evidence indicated that the reaction time varies inversely with body temperature over a restricted range of body temperatures. Possibly when conditions are such that the ambient temperature results in an alteration of body temperature, changes in reaction time may be expected. These conclusions are of practical importance in relation to the duties of submarine personnel in that if it is necessary to expose personnel to extreme temperatures it may predict that they will be able to perform with essentially normal speed, provided the activities are restricted to those kinds of performance involved in the reaction time experiment. Experimental studies upon the effects of cold on the nervous system find practical application also in the use of hypothermia in the treatment of psychiatric disorders as reported by Spradley and Marin-Foucher (*1209*) 1949 and in the application of hypothermia in certain types of surgery.

In profound lethal hypothermia due to cold, death may be a result of the direct effect of cold

upon the heart muscle as stated by Baetjer (*1156*) 1951. Graybiel and Dawe (*1176*) 1948 have reported the case of a previously healthy young man who nearly perished from hypothermia as the result of accidental immersion in ice water. Auricular fibrillation was among the clinical findings. The authors suggested that a possible cause of fibrillation was a local disturbance within the auricles. The cardiovascular effects of brief periods of exposure of human subjects to low temperatures have been reported by Miller and Miller (*1194*) 1949. Sixteen male subjects ranging in age from 19 to 40 years were exposed to temperatures of 34° to −15° F. with no perceptible air movement. Clothing had an insulating equivalent of 1 clo. Subjects were exposed for 20 minutes after sitting in a warm room at a temperature of 70° to 85° F. Adequate sleep and food before cold exposure in these experiments appeared to increase body tolerance. Hemoconcentration was demonstrated in over 75 percent of the experiments. A sudden exposure to cold of moderate to severe degree appeared to be a strong enough stimulation to cause the early mobilization of this protective response. The immediate reaction to cold was a rise in both systolic and diastolic arterial blood pressure, with an early fall in pulse rate.

There is a considerable volume of literature dealing with the effects of low temperatures upon blood flow through the extremities. Spealman (*1206*) 1944 has made blood volume flow measurements on the skin on the hand immersed in water at various temperatures. With water temperatures of 15° to 20° C., there was minimal blood volume flow in the skin of the hand. Skin temperature measurements made at the same time indicated that the difference between skin and water temperature was minimal in immersion in water within these temperature ranges. The effect of increasing the ambient air temperature was to increase this temperature difference, except possibly in the case of very cold water of 10° C. or below. The author concluded that blood flow through the extremities is greater at very low skin temperatures than it is at more moderate skin temperatures. Regarding the implication of these studies to the problem of immersion foot, Spealman felt that it would seem that factors other than ischemia contribute to the development of this condition. Spealman also reported (*1207*) 1945 that at any given temperature of the hands, the colder the body the smaller will be the blood supply to the hands. Calculations from blood-flow determinations revealed that much more heat is supplied to very cold hands than to moderately cold hands, and that the warmer the body the greater amount of heat supplied to the hands. Rapaport,, Fetcher, Shaub, and Hall (*1202*) 1949 have also indicated that the regulation of blood flow to the extremities at low ambient temperatures is primarily determined by the thermal state of the body as a whole. They carried out experiments on four young adult males at controlled ambient temperatures of 0°, −20°, and −30° F. in a cold room. Studies of the exposed bare hands revealed that the vasoconstrictor effects of severe cold is subordinate to autonomic control of blood flow in extremities, since the hand-skin temperature could be sustained above 70° F. Therefore, the temperature of the extremities can remain nearly independent of ambient temperature and of insulation over a wide temperature range, and is dependent primarily upon the thermal state of the rest of the body. Under the circumstances of these experiments in which the body was protected by ventilated clothing, artificial application of heat to the extremities was unnecessary for the comfort of the subjects.

Mead and Bader (*1191*) 1949 reported that when two inactive, seminude men were transferred to a cold environment, a very rapid reduction in blood flow to the fingers and toes, accompanied by a slower fall in skin temperatures, was observed. On return to a warm environment, there was a relatively rapid rise in digital skin temperature while blood-flow return was delayed, the time of onset of return varying with the duration of the prior cold exposure and requiring as long as 2 hours to reach precooling levels after a 2-hour cold exposure. Under these conditions, skin temperature was not even a qualitative index of blood flow, the changes in skin temperature depending largely upon the direct effect of the environment in warming the cooled tissues. In a further study, the same authors (*1155*) 1949 found that nearly maximal levels of blood flow may be maintained in the fingers of an individual otherwise under heat stress in the face of local ambient temperatures that would produce rapid freezing of the digits in cooled individuals. Blood flow through the fingers of an individual otherwise under cold stress may remain relatively low despite local heating of the fingers. When a subject was rewarmed after being cooled, the blood flow returned more rapidly to the fingers which had been maintained in a warm local environment, than to fingers that had been kept in a cold local environment. None of these findings is inconsistent with the view that blood flow through the fingers depends primarily upon the overall body need to conserve or dissipate heat.

In studies carried out by Greenfield and Shepherd (*1178*) 1950, immersion of a finger in a water bath at 0° to 6° C. produced initial, nearly com-

plete, cessation of blood flow. After a few minutes, the blood flow increased notably. Similar but lesser changes in blood flow occurred at 6° to 12° C. and at 12° to 15° C. There was no initial vasoconstriction and the blood flow per minute was lower than in the colder ranges. Cold pain was experienced by the subjects at 0° to 6° C. and this was believed not to be due to steep tissue thermal gradients, but it was postulated rather than vasoconstriction by lowering the internal finger temperature leads to pain.

Further data indicating the dependence of the conditions in the extremities subjected to cold upon the state of thermal balance of the body are provided by papers by Blaisdell (*1159*) 1951; Rapaport, Fetcher, and Hall (*1201*) 1948; and Wyndham and Wilson-Dickson (*1217*) 1951. For further studies of local vessel reactions and body heat emission resulting from immersing the extremities in cold water, papers by Aschoff (*1152* and *1153*) 1944 may be consulted. As Miller (*1193*) 1947 has pointed out, vasodilatation in a part exposed to cold tends to protect that part against freezing. Vasoconstriction in an exposed part permits more rapid freezing. Miller (*1193*) found that chemical vasodilating agents, although capable of producing varying degrees of peripheral vasodilatation in animals with a normal heat reserve, are entirely ineffective in eliciting vasodilatation in a cold-exposed ear of a chilled animal. Such vasodilating agents do not reduce the time or degree of freezing of the exposed ear. This is consistent with the transient vasodilatation produced locally by immersion of the hind limbs of a dog in warm water with the body in a cool room, followed by cutaneous vasoconstriction occurring with continued immersion, Hemingway and Lillehei (*1182*) 1950. It may be concluded that the addition of extra heat to the body of an animal is a much more effective means of achieving peripheral vasodilatation than the use of chemical vasodilators. Miller found that a rabbit having a normal heat reserve can prevent freezing in an ear exposed to a temperature of −55° C. over a period of 2 hours by means of vasodilatation. Miller also found that chemical vasoconstrictors are capable of producing vasoconstriction in an animal having a normal heat reserve to the extent that freezing will occur in an exposed ear within the same length of time as in a chilled animal without vasoconstrictors. Prevention of freezing in exposed areas of the extremities therefore depends upon the maintenance of a normal body reserve of heat and avoidance of factors leading to peripheral vasoconstriction.

For reports on body-temperature regulation under conditions of cold, the following papers should be consulted: Belding, Folk, Forbes, and Darling (*1158*) 1945; Geoghegan (*1173*) 1951; Glickman, Inouye, Telser, Keeton, Hick, and Fahnestock (*1174*) 1947; Hetherington, Luft, Moses, Wilks, Hale, Clamann, Aiken, and Briggs (*1184*) 1951; Malysheva (*1190*) 1950; and Spealman (*1208*) 1949. In discussing heat loss from the body through the skin surface and by way of the respiratory tract, Spealman estimates that heat loss from the respiratory tract may be as high as 50 calories per 1,000 liters of respired air in extreme cold.

The amount of water vapor evaporated from skin in a cold environment is importantly large and may be as high as 19 grams per man per hour in an uncomfortably cold environment and approximately 4 grams less than that evaporated in a comfortable environment. In comfortably clothed men, vaporization of water removes approximately one-quarter of the total heat eliminated from the body. This relationship holds for both active and resting subjects over a wide range of environmental conditions. In cold conditions with peripheral vasoconstriction, approximately 9 calories of heat per square meter of body surface per hour are transferred to the surface of the body for each degree of difference in temperature between the deep body tissues and the body surface. Calculations indicate that the average blood flow in fully vasoconstricted skin is probably less than 15 cu. cm. per square meter of surface area per minute. During moderate vasodilatation, the flow may be 230 cu. cm. per square meter of surface area per minute, and the figure may rise to 1,200 cu. cm. in severe exercise. Heat production in shivering is comparable to that during strenuous work. Men immersed in water up to the neck at 20° C. showed an average heat loss, after body temperature stabilization, of 198 calories per square meter of surface area per hour. The difference in body and water temperature was 15.5° C. Therefore, the heat transferred per degree of difference in temperature was 13 calories per square meter of surface area per hour. Blood-flow values as low as 0.2 to 0.5 cu. cm. per minute have been found in hands and fingers during experiments in moderately cold environments. Extreme degrees of relative ischemia can be withstood for long periods without harm. The blood flow in very cold extremities (5° to 10° C.) is many times greater than flow in moderately cold extremities 15° to 20° C.). Regarding chronic exposure to cold, there has been reported in rats and rabbits a rise in the resting metabolism of 10 to 30 percent, probably the result of thyroid

activation. In human subjects exposed to a temperature of 15° C. for about 2 weeks, there was a 7-percent rise in basal metabolic rate on the average.

Numerous studies have suggested that hemodilution occurs in hyperthermia and hemoconcentration occurs in hypothermia. These deductions have been inferred from changes in the osmotic pressure or the plasma-protein concentration of the blood. Rodbard, Saiki, and Malin (*1203*) 1950 stated that so far as they were aware no data were available on the actual changes in blood volume and its relation to changes in the extracellular and intracellular fluid compartments. Their studies on physiological effects induced by body temperature changes were therefore extended to investigate possible fluid shifts in order to assay more adequately the effects of low temperature upon the cardiovascular system. In these experiments, rabbits and chicks were used as experimental animals. Lowering the body temperature to 25° C. resulted in only a slight increase in hematocrit and specific gravity. However, plasma and blood volumes and thiocyanate space were all reduced 30 percent below normal levels. Rewarming resulted in a return to normal values. Induced hyperthermia caused a slight decrease in hematocrit and plasma specific gravity. Plasma and blood volumes were slightly reduced, but thiocyanate space was increased as much as 30 percent. These data suggested to the authors that induction of hypothermia results in a shift of fluid from the plasma and the interstitial spaces to the intracellular phase. The fact that the hematocrit and specific gravity do not rise commensurate with the decreased volumes suggests that blood cells and plasma proteins are removed from the circulating plasma and stored. The reverse processes are brought about by rewarming to normal temperature levels. Induction of hyperthermia causes water to leave the tissue cells, and causes commensurate quantities of plasma protein and blood cells to be released to the circulating bloodstream.

Miller (*1192*) 1949 has reported a study of certain blood properties in healthy young men transferred from a subtropic to a subarctic environment. Thirty volunteer subjects were heat adapted during July, August, and part of September 1947 at Randolph Field, Tex. In the latter half of September, the subjects were transferred to Ladd Field, Alaska, via train and ship. The lowest environmental temperature encountered was −40° F. The living quarters at Ladd Field were adequately heated. In these subjects complete blood studies were done both at Randolph Field and at Ladd Field. These included erythrocyte and leukocyte counts, differential white counts, hematocrit ratios, coagulation times, sedimentation rates, specific gravity of whole-blood plasma, blood-sugar levels, total blood-protein levels, and fasting serum chloride levels. The experimental results revealed no marked changes in the blood properties investigated, although there was the general tendency toward increase in red cell counts. All other differences were slight. The author concluded that the studies offered no evidence for the occurrence of acclimatization to cold for the factors studied. A further study on the mechanism of acclimatization to cold and loss of heat acclimatization in men subjected to prolonged cold exposures has been reported by Stein, Eliot, and Bader (*1210*) 1949. Three healthy, unacclimatized, white males were intermittently exposed successively to a 2-week period of physical conditioning followed by 19 periods of heat lasting 5¼ hours each. Following this, there were fourteen 5-hour periods of cold at −20° F. with a wind velocity of 3 or 4 miles per hour. There were then 5 exposures to heat followed by a 5-week interval of no exposures to environmental stress, and finally 3 reexposures to heat. Throughout the entire experimental period, measures were made of cardiovascular and metabolic function, water and chloride balance, and body-water partition. The results of the study indicated that in heat-acclimatized men, no acceleration of deacclimatization is caused by repeated, intermittent exposures to cold. Acclimatization to heat may be maintained for periods of several months by occasional reexposure to the original environmental stress. Toe temperatures during repeated cold exposures decreased more rapidly with successive exposures suggesting more rapid and complete vasoconstriction, which does not necessarily represent acclimatization to cold since no increased tolerance to cold was demonstrated. Marked diuresis and negative chloride balance were observed throughout the period of cold exposures, tending to persist during subsequent reexposures to heat. No significant differences in total blood plasma or thiocyanate space volumes were found in any of the experimental periods, although plasma proteins and hematocrit values suggested hemodilution in heat and hemoconcentration in cold. The finding that heat acclimatization can persist even with fairly severe cold exposures intervening suggested to the authors that acclimatization to cold may be accomplished in part by mechanisms different from those involved in heat acclimatization. It may be that many of the fundamental changes which occur are the same in both types of acclimatization and one may actually reinforce the other.

For a report on the effect of local cooling on fluid movement, effective osmotic pressure, and

capillary permeability, a paper by Brown and Landis (*1162*) 1947 may be consulted.

The effects of cold on the air passages and the lungs have been reported in papers by Moritz and Weisiger (*1196*) 1945 and Webb (*1216*) 1951. The former authors caused dogs to breathe extremely cold air for periods ranging from 20 to 130 minutes. The temperature of the air delivered to the larynx ranged between −50° and −28° C., and in no instance were the temperature readings lower than +18° C. at the bifurcation of the trachea, inhalation of cold air in circumstances such that intralaryngeal inspiratory temperatures as low as or lower than −30° C. were reached resulted in the development of a localized sublaryngeal tracheitis. In some adults, the disturbance was limited to unusual activity on the part of the mucous secreting glands, and in others, there was focal destruction of the superficial epithelium. There was no evidence of injury to the lower part of the trachea, to the bronchi, or to the lungs. According to the authors, the explanation of the rapid warming of inhaled cold air and of the occurrence of the relatively mild and localized injury following inhalation of cold air lies in the fact that dry air has an extremely low heat capacity and that the number of calories required to produce a great rise in the temperature of dry air can be provided by the heat derived from the cooling of a small amount of tissue by a few degrees. Long exposure to cold air, according to the authors, might result in obstructive edema. Webb also measured the air temperature in the airway with a thermocouple and made air temperature tracings from the front, middle, and the back of the nose from 18 resting human subjects in the following ambient air temperature ranges: 23° to 28° C., 5° to 8° C., and −20° to −31° C. Average minimum peak temperatures from these records demonstrated that the inspired air was rapidly warmed in its passage through the nose. At the back of the nose, inspired, warm ambient air had reached a temperature of 31.7° C.; cool air had reached a temperature of 30.0° C.; and cold air had reached a temperature of 25.4° C. Average maximum temperature peaks demonstrated that expired air at the back of the nose did not exceed 35.5° C., 34.9° C., and 31.9° C. at warm, cool, and cold ambient temperatures respectively. Measurements at the front of the nose showed that average maximum expired air temperature peaks had dropped to 34.1° C., 29.2° C., and 26.2° C. under the same respective conditions.

Grayson (*1177*) 1949 found that general body heating produces a vasoconstriction in the human bowel followed by a vasodilatation. His same techniques were used to investigate the effects of limb cooling. When the arm was immersed in ice water, a variable and transient vasodilatation of the bowel occurred at first and was always followed by a pronounced vasoconstriction and a fall in body temperature. With the circulation to the arm occluded, immersing the limb in ice-cold water always produced a marked vasodilatation. On releasing the occluding pressure with the arm still in the water, a rapid fall in body temperature and a pronounced vasoconstriction in the bowel occurred. Vasoconstriction was never observed in response to limb cooling while the circulation to the limb was occluded. The vasodilator effect of cold on the bowel circulation was, therefore, not conceived to be the result of direct cooling of the blood. The effect of circulating cooled blood appeared, in fact, to act as a vasoconstrictor stimulus so far as the bowel is concerned. In experimental studies, Cordier and Piery (*1165*) 1950 studied the influence of cold on the speed of transit and intestinal absorption of glucose solutions in the rat. These animals were exposed to a temperature of −5° C. Exposure to this low temperature resulted in an acceleration of glucose movement in the stomach and an increase of intestinal absorption of glucose. This was ascribed by the authors not to an increased epinephrine secretion but to hypersecretion of the thyroid gland. In a study of nutritional requirements for men at work in cold, temperate, and hot climates, Gray, Consolazio, and Kark (*1175*) 1951 measured the caloric output of men doing hard work in these three different environments while wearing standard Arctic, temperate, and desert clothing. The subjects were healthy university students in excellent training. Their daily dietary intake exceeded the National Research Council's recommended daily allowance for protein, calcium, phosphorus, irons, vitamin A, thiamin, riboflavin, niacin, and ascorbic acid. Their protein intake was largely of animal origin and their caloric intake was equal to their needs. Measurements of basal metabolic rate work output, oxygen consumption at work, and differences in body weight before and after exercise were made daily. The results of these studies showed that the caloric output for a given amount of external work performed at a constant temperature increased about 5 percent when the clothing was changed from desert clothing and increased above 5 percent more when the clothing was changed from temperate to Arctic clothing. The caloric output for a given amount of external work performed in a given outfit of clothes decreased about 2 percent as the temperature was raised from −15° to 60° F., and de-

creased about 2 percent more when the temperature was raised from 60° to 90° F.

In 1950, Swain, Toth, Consolazio, Fitzpatrick, Allen, and Koehn (*1212*) estimated the voluntary food consumption of troops at Fort Churchill during three 10-day periods in the winter of 1947–48. This location was chosen because it has about the highest wind-chill value of any inhabited area. The troops spent about 3 hours every day in the open. Food consumed in the messes was recorded and plate wastes were weighed. An attempt was made to estimate canteen food. An abundant ration of fresh and frozen food was provided, averaging 5,500 calories per man per day. In these studies, all nutrient intakes equaled or exceeded the recommended allowances of the National Research Council for an active man. Continuous weight records of a small number of men showed a slight, mean rise during this period. It was concluded that the caloric intake varied inversely with the mean environmental temperature, and was directly correlated with the mean wind chill. There was no preference for fats in the subarctic climate and the percentages of calories provided by protein, fat, and carbohydrate were about the same as those in temperature climates, being 13, 40, and 47 percent, respectively. It appeared that the troops regulated their food intake in relation to the severity of the weather, but it seemed that their appetite for particular foods was not altered. Mitchel and Edman (*1195*) 1951 also concluded that cold environment in proportion to severity definitely increases caloric requirements of men. Water requirements were stated to be depressed except as sweating may occur during severe work in heavy Arctic clothing. Dietary modifications may definitely affect tolerance to cold. A high carbohydrate diet was stated to be superior to a high protein diet. The addition of dietary fat improves the relatively beneficial effects of carbohydrate. Tolerance to cold did not seem appreciably to be improved by the addition of thiamin, ascorbic acid, riboflavin, and niacin in proportions adequate in a comfortable environment. It was concluded that the extra calories required in cold were better supplied by increasing the carbohydrate intake and the fat intake rather than by increased proteins. The extent to which this can be put into effect in feeding communities of men depends upon acquired food habits, the duration of residence in Arctic environments, the motivation for such residence, and the extent to which a diet can be made palatable. In conditions of inactivity, high-protein intake may exert a temporary, favorable effect upon cold tolerance. The authors believed that decreasing the intervals between meals, especially if the foods are rich in fat, may increase the favorable effect on thermal balance in cold environments. The authors warned that the results of animal experiments are not applicable to man and should not be applied to human situations before actual field tests on human subjects. For a further study of diet at low temperatures with particular reference to fat utilization, a paper by Butson (*1163*) 1950 may be consulted.

Reference may also be made to 3 animal studies on the relation of low environmental temperatures to diet by Donhoffer and Vonotsky (*1167*) 1947, Ershoff (*1170*) 1950, and Hegsted and McPhee (*1181*) 1950. Donhoffer and Vonotsky reported an increase in food consumption in white mice at low temperatures (10° to 11° C.) and a decrease at high external temperatures (29° to 33° C.). It appears from the studies of Ershoff that prolonged exposure to cold increases the vitamin A requirements of the rat. Immature rats were fed purified rations deficient in vitamin A under cold-room conditions (2° C.) and room temperature conditions (23° C.). The rats became depleted more rapidly under the cold-room conditions than under ordinary room conditions. The body weight at the time of depletion was less in the cold-room rats than in the ordinary room temperature series, and finally the length of survival after depletion was significantly decreased in the cold-room series. Hegsted and McPhee found that there was an increased thiamin requirement in rats under cold-room conditions.

Regarding the effect upon metabolic rate and heat output of exposure to cold in human subjects, Forstenberg, Newburgh, and Spealman (*1172*) 1944 reported a slight increase in both basal metabolism and total heat production after 10 days in a group of lightly dressed men who lived in a room at a temperature of 15° C. for 4 weeks. This temperature was low enough to cause distinct discomfort, but not cold enough to produce shivering. In some subjects, the increase in metablic rate lasted for some days after the experiment was concluded. This delayed response was attributed to a possible late period of thyroid response. A slight lowering of blood cholesterol levels was noticed. Discomfort gradually lessened or disappeared. This was not due to a change in skin temperature or increase of heat production. Energy exchange data were obtained by Frantz and Roth (*1171*) 1948 on human subjects residing continuously for 9 days in a cold environment at a temperature of −32° C. The subjects fasted in the same environment for a period of 6 days to provide control data. Clothing assemblies

and sleeping bags were adequate to maintain normal body temperature and comfortable skin temperature without the necessity for fatiguing exercise during fasting or subsistence upon the ration. The ration used was the USAF emergency ration. Progressive limitation of voluntary activity was noted in the fasting subjects. The respiratory quotient approached 0.72 with continued fasting, especially for exercise requiring more rapid caloric expenditure. The metabolic cost for a standard workload on the treadmill was increased during low-temperature exposure. This was not observed during the activities in which the hobbling effect of the clothing did not participate, that is to say, lying, sitting, and standing quietly. Considering ability to perform psychomotor tasks, gross work capacity, and maintenance of body comfort in the fasting and nonfasting subjects, food appears to be of secondary importance to the adequacy of clothing and sleeping bags for survival at low ambient temperatures.

In 1947, Horvath and Golden (*1185*) reported observations on men performing a standard amount of work in low ambient temperatures. Five subjects wearing light and heavy clothing walked at a standard rate of speed and grade of climb on a motor-driven treadmill in comfortable and very cold environments. The energy expenditure for the standard work was increased by 10 percent in the lower ambient temperatures. This increase seemed to be independent of the amount of clothing worn. Ability to work was not signficantly impaired even at ambient temperatures as low as −46.7° C., although there was a slight decrease of mechanical efficiency at certain of the environments. The loss of body heat was greater with the lightweight clothing, and the magnitude of the loss appeared to be directly related to the ambient temperature. Heat debts were less but quite variable when heavy clothing was worn. In all cases, the heat debts were accumulated in the early portion of exposure to the cold environment.

Observations of metabolic rate, and skin and rectal temperatures of men exposed to extremely cold environments, have been made by Horvath, Golden, and Wager (*1186*) 1946. The experiments were carried out on 45 men dressed in Arctic uniforms and sitting quietly in ambient temperatures ranging from 1.1° to −40° C. The heat production in the cold was observed to be above basal values during the entire test period. In the −40° C. environment, average metabolic increases of 13, 53, and 74 percent were recorded for the first, second, and third hours, respectively. The rise in heat output during the first hour could not be explained on the basis of shivering. In the third hour, shivering was present in the majority of the subjects. The fall in rectal temperatures was moderate, although low values of 35.4° C. were occasionally observed. The absolute value was not correlated with the presence of shivering, and low rectal temperatures could not be considered as the stimulus for shivering. Mean skin temperatures fell precipitously during the first hour of exposure and became stabilized before the end of the test period. Considerable variability was observed in both the rate and the extent of the fall, notably in different subjects but also in repeat tests on the same subject. Of all the skin areas, hands and feet exhibited the greatest temperature changes in both rate and degree of fall. Toe temperatures below 0° C. were observed in several instances. The susceptibility of the extremities to cold environments was related to their sensitive vasomotor mechanisms, and to the fact that they were provided with the least amount of insulative protection. The responses of men exposed to cold environments are subject to considerable variation, and extreme care must be exercised in the interpretation of data obtained, whether on a few or a large number of subjects.

Although some authors have reported that exposure to cold increases the basal metabolic rate, it has been found by Ames and Goldthwait (*1151*) 1948 that the basal metabolic rates of 10 out of 11 subjects moved from Lawrence, Mass., to winter quarters at Churchill, Manitoba, Canada, were not apparently affected by the change in environment. However, the basal metabolic rate of one subject increased during the winter at Churchill, possibly as a result of exposure to cold. This subject received more exposure than any of the other ten, averaging 5.1 hours a day out of doors. Contrasts between men and women in basal heat production and heat loss during exposure to environmental temperature extremes have been reported by Hardy, Ebaugh, Stevens, and DuBois (*1180*) 1950. Thirteen normal young women were studied in the respiration calorimeter of the Russell Sage Institute of Pathology. They were under basal conditions and nude. Measurements were made of gas exchange, rectal and skin temperatures, total heat loss, and percentages lost by radiation, convection, and vaporization. On different days they were exposed to calorimeter temperatures in the range between 22° and 35° C. In the cold zone, even before the appearance of significant muscular tension or chills, there was often found a slight rise in heat production, suggesting a chemical regulation of metabolism. In 5 of the subjects, this was absent, but in 4 it was slight and in another 4 it was distinct. This was in contrast to the basal metabolism of men, which usually remains

constant in the cold until the abrupt onset of a chill. Some of the women showed a prolonged rise in metabolism with the onset of chill much later than in the case of the men. Some women appear to have a regulation of the balance between heat production and heat loss which is more adaptable than is usually found in male subjects. In 45 test subjects taking part in the test of the experimental Arctic Trial Ration (AT–1) in the vicinity of Fairbanks, Alaska, from 12 February to 4 March 1950, Sargent and Consolazio (*1204*) 1951 found no significant alterations in water or electrolyte balances. Albumin and sugar levels were observed in the urine only occasionally, and then in trace quantities. The significant biochemical finding was ketonuria. Changes in ketonuria observed during the Army ration trials were considered to be manifestations of the general adaptation syndrome, and alterations in ketone body metabolism are suggested by the authors as a means of investigating the metabolic aspects of adaptation to cold. As Brolin (*1161*) 1946 has stated, exposure to low temperatures is believed to produce an increased activity of the thyroid gland and the adrenal cortex. The response of the thyroid gland to a low environmental temperature has been studied by the use of radiactive iodine by Schachner, Gierlack, and Krebs (*1205*) 1949. Wistar-strain male albino rats were exposed to about 4° C. for periods from 2 hours to 60 days, and the percent uptake of radioactive iodine by the thyroid glands measured. At exposure periods under 3 hours, there was a diminished amount of radioactive iodine present in the experimental animals, while the amount present in animals exposed about 6 hours was the same as for controls. There was an increase in radioactive iodine uptake after 12 to 24 hours' exposure. This increased iodine uptake was most pronounced at 7 to 9 days, and then gradually returned to control values after 40 days. Tobin and Steeples (*1214*) 1942 found that in rats exposed to cold, there was a decrease in the cholesterol content of the adrenal glands. Male rats were more resistant to cold than were the females. The decrease in adrenal cholesterol was found to be less in heavier animals than in lighter ones exposed to the same low temperature. Administration of an aqueous adrenal cortical extract produced a diminution in the fall of adrenal cholesterol in all rats exposed to low temperatures. Dugal and Thérien (*1168*) 1949 found a typical enlargement of the adrenal glands in rats and guinea pigs exposed to cold. This enlargement of the glands was completely prevented by large doses of ascorbic acid. Ascorbic acid seems to play a compensatory role similar to adrenal cortical hormones. Not only was hypertrophy of the glands prevented, but also resistance to cold was increased. According to Hermann, Chatonnet, and Vial (*1183*) 1949, rats exposed to cold (2° C.) for periods ranging from 15 minutes to 2 hours showed a decrease in the epinephrine level in the adrenal glands proportional to the length of exposure. This was ascribed to the excessive secretion of the hormone and implying a drainage of the gland. According to Osgood and Gimmerman (*1198*) 1949, the 17-ketosteroid excretion of seven healthy male subjects was not significantly changed during a field exercise at Fort Churchill, Canada, under conditions of extreme cold from the levels of excretion recorded for the same men during a similar exercise under temperate climatic conditions at Fort Knox, Ky. A diurnal variation in 17-ketosteroid excretion was observed in these subjects, the hourly excretion during the waking hours being consistently greater than that during sleep. These studies seem to indicate that the subjects may have already been adapted to the stress of cold and exercise during the period at Fort Churchill prior to the first urine collections.

Renal and hormonal mechanisms of cold diuresis have been reported by Bader, Eliot, and Bass (*1154*) ·1949. Men were exposed at 15° C., reclining nude except for shorts. Results on these subjects were compared with results of exposure at 24° to 27° C., the subjects being covered by blankets. Endogenous creatinine clearances in nine experiments showed no significant change in glomerular filtration, and in 16 experiments there was no significant change in either endogenous creatinine or para-aminohippuric acid clearance during cold diuresis. In 12 experiments, there was a substantial reduction in cold diuresis during standing, as compared with reclining. Cold diuresis was inhibited following 15 minutes of walking. During cold diuresis, the specific gravity and chloride concentration of the urine fell as the volume rose, and each change appeared to be correlated with the previous state of hydration and chloride content of the diet. Use of an index of chloride reabsorption showed that chloride tended to be reabsorbed to a greater degree than water. In 27 experiments, 3 subjects received small intramuscular doses of either 0.015, 0.03, 0.06, or 0.12 units per kilogram of body weight of pitressin at the beginning of each exposure, either cold or warm. Inhibition of cold diuresis was proportionately longer lasting following the larger doses, but even the smallest dose reduced urine flow for 1½ hours to the same small output seen in the warm exposures, with or without pitressin. The strong similarity between water and cold diuresis and the extreme sensitivity to pitres-

sin were presented by the authors as suggestive evidence that cold diuresis is controlled by the posterior pituitary gland. The same authors (*1169*) 1949 alternated the order of exposure (2½ hours) to 27° C. and 15° C. between men and in each man from day to day. In 23 experiments, plasma proteins rose an average of 0.5 gram per 100 cu. cm. and the hematocrit rose 2.9 percent in the cold. In 12 experiments, the corrected sedimentation rate rose 76 percent in the cold. When warm exposure followed the cold, these values fell an average of 0.5 gram per 100 cu. cm., 1.8 and 41 percent, respectively. In 18 experiments on 5 men, the average increase in urine output in the cold over output in the warm was 287 cu. cm., which corresponded to an average plasma loss of 277 cu. cm. as calculated from increase in plasma proteins, hematocrit, and an estimated plasma volume of 50 cu. cm. per kilogram of body weight. In a series of 15 experiments, cold diuresis was largely or completely abolished by the small doses of pitressin, but the plasma proteins rose 0.4 gram per 100 cu. cm. and the hematocrit rose 2.6 percent, indicating that there is no direct connection between changes in urine output and plasma volume in the cold. Further evidence of the role of the pituitary gland in cold diuresis has been provided by Stutinsky (*1211*) 1949. The reader is also referred to a report by Talso, Crosley, and Clarke (*1213*) 1947, in which it was shown that the cold pressor test in 6 out of 7 normal, male subjects resulted in a reduction of glomerular filtration rate and effective renal plasma flow. These changes occurred either during the application of the local cold stimulus, or within approximately 30 minutes thereafter.

An important effect of cold is the stiffness in joint movements which may result in a loss in manual dexterity. For an experimental study of the factors responsible for joint stiffness in cold, a paper by Hunter and Whillans (*1187*) 1951 should be consulted. In experiments on the knee joint of the cat, stiffness was present under conditions of zero and subzero temperatures even after the joint had been freed from muscular attachment, with exception of the cruciate ligaments. It would appear, therefore, that a physiologically important component of joint stiffness resulting from exposure to cold must result from a local physical change in the joint tissues with an increase in friction of the joint. A final point of physiological importance concerns the relation of cold tolerance to age. De Boer and Ederstrom (*1166*) 1946 reveal that young puppies about a week old have a much greater tolerance to hypothermia than adult dogs. This is generally true for all animals.

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C. CHILBLAINS

Chilblains may constitute a problem in submarine personnel under conditions of operation in cold, damp environments. Chilblains are due to defective peripheral circulation. Sites of election are the fingers, the ulnar sides of the hands, the great toes, the heels, and the ears. Simple, first-degree chilblains are round, oval, or variably shaped macular areas which may be livid red or bluish in color. The skin is shiny and appears thin. There may be discomfort, pain, smarting, itching, cramp, and coldness. In second-degree chilblains, the skin may be broken or ulcerated, the swelling more intense, and the erythema more pronounced. There may be mottled and livid plaques. The lesions are painful and sometimes a sero-purulent liquid is found. Following healing there may be scars. Wigley (*1219*) 1946 has stressed the importance of warm clothing and the use of loose gloves and boots. The feet should be kept dry with frequent changes of socks. Cold-water baths should be avoided and tepid water used instead. The feet may be washed with weak potassium permanganate. The author recommends various sedative solutions and suggests that penicillin cream may be used for ulcerated chilblains. Gourlay (*1218*) 1948 has recommended the use of nicotinic acid in the treatment of chilblains. The adult dose by mouth is 50 mg. 3 times a day after meals. Gourlay reported a high percentage of cure of chilblains and stated that some patients reported an increased tolerance to cold. It was suggested that nicotinic acid be taken at the first sign of chilblains and continued until the cold, damp season has passed.

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D. ACCLIMATIZATION AND TOLERANCE TO COLD

Tolerance to cold has been shown to be related to age in experimental animals. Adolph (*1221*) 1951 and Adolph and Lawrow (*1222*) 1951 have shown in the cat, the golden hamster, and rat, and to some extent in the mouse, guinea pig, and rabbit that newborn animals will endure lower temperatures than older animals. There are also species differences in cold tolerance amongst the different laboratory animals, and Fetcher (*1235*) 1948 has shown that adult guinea pigs do not tolerate as severe reductions of body temperature as do adult rats. The former die at colonic temperatures of 17.5° to 21° C. while the latter survive at a colonic temperature as low as 15° C.

Vascular responses, principally of the fingers, and their relationship to cold tolerance have been investigated by Bader and Mead (*1227*) 1949 and (*1224*) 1950. A variety of vascular responses were observed in a group of 24 men and compared with an evaluation of certain aspects of their individual cold tolerance. These studies were carried out under

controlled ambient conditions and at Fort Churchill, Manitoba, Canada. Individuals in whom reduction of finger blood flow during immersion of the feet in ice water was relatively transient showed, in general, a lower incidence of frostbite. They were able to work with unprotected hands in the cold for more prolonged periods than those in whom vasoconstriction was maintained throughout immersion of the feet in ice water. The authors stressed that, although correlation between digital vascular response and cold tolerance was demonstrated for certain experimental groups, there were notable individual exceptions to the pattern. Hence, the cold-immersion response of a particular subject cannot be regarded as a specific indication of his performance under cold stress. No other physiological indices investigated were shown to have a significant relationship with cold tolerance. These indices included spontaneous variations in finger-pulse volume and finger mean volume during the control period, finger-pulse reduction during the warming phase prior to cold immersion of feet, maximum finger-pulse-volume reduction during immersion, blood-pressure rises during immersion, and severity of pain experienced during immersion. Men studied before and after a field bivouac under cold stress experienced less pain and had smaller blood-pressure rises during immersion of the feet in ice water after bivouac. These changes were not observed in a control group.

As has been pointed out by Booker, Dent, Jones, Hudson, and Hayes (*1228*) 1951, the mechanisms involved in protection against and recovery from various stresses such as cold remains largely an unanswered question. That the adrenal gland is in some way related to ascorbic acid metabolism in normal and in stressed condition is well known, although exactly what the relationship is cannot at present be explained. In an attempt to derive information which might throw more light on these questions, the authors subjected adrenalectomized mice in a cold room to a temperature of 42° F. along with mice of approximately the same weight and sex with the adrenals intact. The survival time of the two groups was studied. The role of ascorbic acid, cortisone, and ACE, separately and in combinations, was studied. The results show that ascorbic acid in low and in high doses is not effective in increasing the survival time of adrenalectomized animals. Both cortisone and ACE are effective in increasing the survival time of the animals in the cold room appears to be an important factor. Combinations of cortisone and ascorbic acid, and ACE and ascorbic acid were found to be more effective than the steroids alone in increasing the survival of the mice in the cold.

Lange, Gold, Weiner, and Kramer (*1244*) 1948 found that rabbits restricted in their activity have a definitely shortened survival time compared with unrestricted controls when exposed to a temperature of −20° C. The restricted animals were unable to maintain a normal body temperature even when in the first few minutes of exposure the temperature drop was in a straight line. Superficial anesthesia simulating sleep also resulted in a more rapid loss of body temperature than occurred in the controls. Inebriating doses of alcohol likewise reduced survival time. Treatment with thyroid hormone for several days before exposure resulted in a striking prolongation of survival time. Partial suppression of thyroid function by thiouracil lead to a more rapid fall of body temperature and a shortening of the survival time. There was a lag of 3 or 4 days before the protective effect of oral, subcutaneous, or intravenous thyroid medication became noticeable. These findings regarding the effect of thyroxin are consistent with those of Turner (*1252*) 1946 who found that administration of thyroxin decreased the hypothermia of mice subjected for 1 hour to an environmental temperature of 5° C. In Turner's experiments, administration of dinitrophenol in doses calorigenically equal to the thyroxin exaggerated the hypothermia.

The effects of dietary modifications upon the tolerance of man to cold has been investigated by Keeton, Lambert, Glickman, Mitchell, Last, and Fahnestock (*1243*) 1946. The subjects were divided into two groups, the first receiving a high protein diet for 5½ months and the second a high carbohydrate diet for the same period. The daily food intake was consumed in four meals. The cold room was kept at −20° F. The subjects were clothed in Army Quartermaster Corps Arctic clothing and the following measurements were carried out: rectal and skin temperatures, and psychomotor and visual efficiency tests such as critical fusion frequency of flicker, visual choice reaction time, speed of tapping, coordination time, and normal steadiness in holding a stated position and during voluntary movement. The following conclusions were derived from the data: There was an incomplete inversion of diurnal rhythm of physiological functioning in subjects recently changed from normal daytime to nighttime activity. High-protein diet was associated with the excretion of larger amounts of creatinine in the urine, but there were never any signs of kidney damage. The heat increment, that is to say, the specific dynamic effect of high-protein diet, was 50 percent greater than for the high-carbohydrate diet

during 6 hours post prandium under cool conditions, and 76 percent greater under comfortable environmental conditions. Subjects on high-protein diet required for the maintenance of body weight an average total caloric intake of 162 percent of basal energy expenditures. For subjects on a high-carbohydrate diet, the figure was 191 percent. More complete protection by clothing of the trunk, upper arms, and thighs will retard the cooling of the body and of the skin, but not of the extremities during cold exposure. More complete clothing protection also obliterates the dietary effects on cold resistance. Additional clothing was found to retard the rate at which performance of psychomotor tests are adversely affected by cold, but only for the high-carbohydrate diet. Cooling of the internal body tissues on exposure to intense cold was greater on the high-protein diet. High-carbohydrate diet was found more potent in combating the effects of intense cold by slowing the rate of surface skin cooling. High-carbohydrate diet, more than high-protein diet, lessens the adverse effect of intense cold on psychomotor performance. The superiority of the high-carbohydrate diet over the high-protein diet in increasing tolerance to cold of adult men under conditions in which caloric requirements are just satisfied is associated with and probably causally related to increased requirement of food energy and presumably increased heat production. It is not related to the differential specific dynamic effects of diets as revealed during the 6-hour period post prandium. In a further study, Mitchell, Glickman, Lambert, Keeton, and Fahnestock (*1247*) 1946 investigated the tolerance of man to cold comparing the values for carbohydrate diets versus high-fat diets and the effect of frequency of meals. Subjects given high-carbohydrate diets in the experiments reported above (*1234*) were given high-fat diets in the present experiments. Those given high-protein diets in the previous experiments were given high-carbohydrate diets in the present study. All subjects were lightly clothed, that is to say, they did not wear fleece innerliner or the cotton-hooded parka, but wore all other warm clothing. It was concluded that the high-fat diet induced a mild ketonuria, but no hemolysis in blood samples taken under basal conditions. For the maintenance of body weight, the subjects on high-carbohydrate diet required a total caloric intake of 188 percent of basal energy expenditures. Those on high-fat diet required 200 percent. Cooling of the internal tissues of the body on exposure to intense cold was greater in the subjects on high-carbohydrate diet, but only when the interval between meals was reduced to 2 hours. Regarding cooling of the skin, there was no superiority of high-fat diet over high-carbohydrate diet in subsequent 4-hour periods of exposure to cold. It appeared highly probable that the high-fat diet was superior to high-carbohydrate diet in maintaining general psychomotor performance and visual efficiency. The fat diet was clearly superior to the carbohydrate diet in speed of tapping. Decreasing the interval between meals during cold exposure had no favorable effect on rectal temperature changes if the meals were largely carbohydrate, but there was a definitely favorable effect with high-fat meals. Decreasing the interval between meals progressively and strikingly increased the favorable effect on the maintenance of psychomotor functioning, but obliterated the differential effects produced by diets differing widely in proportions of fat and carbohydrates. The character of the meal consumed just prior to cold exposure exerted no appreciable effect upon the maintenance of psychomotor performance during exposure. The superiority of high-fat meals in maintaining tissue temperature in cold environment is related to heat emission, and not heat production, and may involve a temporary deposition of dietary fat in the subdermal tissues following high-fat meals. It was concluded generally that dietary modifications may exert favorable effects upon the ability of man to withstand exposure to intense cold. High-fat and high-carbohydrate foods are preferred to high-protein diet, and small meals every 2 hours are considered better than large meals at 4 to 6 hours' intervals.

Glickman, Keeton, Mitchell, and Fahnestock (*1240*) 1946 also investigated the effects of intake of water-soluble vitamins on the tolerance of man to cold. The experiments were carried out on 12 healthy young men over a 150-day period to determine the effect of supplements of water-soluble vitamins to diets containing only borderline concentrations of these vitamins. The cold stress was repeated exposure of 8 hours' duration either to intense cold (−20° F.) with considerable protective clothing or to a cool environment (60° F.) with little protective clothing. The basal diet consumed by all the subjects was considered adequate according to current standards in all essential nutrients except ascorbic acid, thiamin, riboflavin, and nicotinic acid. The amounts of these vitamins in the basic diet was generally two-thirds or less than the recommended allowances of the National Research Council Food and Nutrition Board. The daily vitamin supplement consisted of 200 mg. of ascorbic acid, 8.8 mg. of thiamin, 8.0 mg. of riboflavin, 120 mg. of nicotinamide, 10.2 mg. of pyriodoxine, and 20.4 mg. of pantothenic acid. When not receiving

vitamins, the subjects received placebos indistinguishable from the vitamin capsules. At no time were there clinical symptoms referable to the experimental diets, and no biochemical evidence that the vitamin levels of the basic diet were inadequate for normal nutrition for the 89-day period. The results of the study clearly indicated to the authors that the ability of men to withstand the damaging effects of repeated exposure to cold environments and maintain normal neuromuscular mental efficiency was not appreciably enhanced by supplementary doses of ascorbic acid, thiamin, riboflavin, nicotinamide, pyridoxine, and pantothenic acid in the amounts given in these experiments. A summary of these experiments is to be found in an unsigned article (*1253*) published in 1946. Similar conclusions have been expressed by Mitchell and Edman (*1246*) 1949. These authors express doubts that animal experimentation in this field of research may yield profitable results applicable to man's situation. Animal studies reported by Ershoff and Greenberg (*1234*) 1950 indicate that deficiency of vitamin A in rats may impair the ability of rats to withstand subsequent exposure to cold. Vitamins, including vitamin A, added to the diets of these animals may improve tolerance to cold.

For a report of a nutritional investigation on British naval personnel under cold climatic conditions at sea, reference may be made to a paper by Geohegan and Sinclair (*1237*). 1949. In these studies, there was a significant loss of body weight among the men who were exposed to cold conditions, but none among those not exposed. Age was not a factor in the loss of weight. The daily caloric consumption was 3,800 calories. This diet seemed adequate in vitamins and minerals. Under cold climatic conditions, a diet of not less than 4,300 calories was recommended for all personnel. For personnel exposed for 4 or more hours daily it was considered that there should be given an additional meal of 1,000 calories. For watchkeepers, the authors recommended an increase in the diet of one-half ounce of sugar per man per watch.

As Gladwin (*1239*) 1947 has stated, adaptation to extreme cold involves cultural devices as well as physiological adjustments. Studies by Bly, Johnson, Kark, Consolazio, Swain, Laudani, Maloney, Figueroa, and Imperiale (*1226*) 1950 suggest that during the first few days of abrupt exposure to cold, unacclimatized soldiers exhibit a general adaptation syndrome, with stimulation of the pituitary-adrenocortical system. According to Miller and Pecora (*1245*) and Pecora (*1248*) 1948, there is no impaired renal function in men living in a subarctic environment under ordinary circumstances with a sufficient caloric and fluid intake. If the fluid and food intake is inadequate, there may be evidence of temporary renal dysfunction. Renal stress may be accentuated by living under the strain of a severely cold environment. Abnormal urinary constituents disappear as soon as men returned to a warm situation. Red cell counts showed an increase in men transported from Texas to Alaska, and hematocrit levels tended to decrease. There was also a decrease in mean corpuscular volume. Sedimentation rates showed no particular direction of change, and coagulation times tended to increase. There were no changes in the electrocardiogram of men exposed to short periods of severe cold. The diurnal temperature cycle seemed to be oriented at a somewhat lower level in men living in the subarctic as compared with cycles in the subtropic environment. From hand calorimeter studies on all the subjects, it could be said in general that men transferred from subtropic to a subarctic climate showed a decrease in the amount of heat loss through their hands. There were no significant changes in the basal metabolic rates in subjects transferred from Texas to the subarctic environment, although the Eskimos were found to have a generally increased basal metabolic rate.

Change in the circulation of blood in the extremities as a factor in acclimatization to cold was discussed by Bazett (*1225*) 1949. He pointed out that seamen on long exposure to cold weather at sea become able to withstand immersion of the hands in water much better than do other individuals. It has not been established whether the local surface temperature of the exposed surface is allowed to fall to lower temperature levels or whether vascular reactions are exaggerated and maintain abnormally high temperatures. The skin of acclimatized subjects appears to be thicker and coarser than that of unacclimatized persons. It is possible that the tissues develop a capacity to withstand cooling so that deeper tissues can attain a somewhat lower temperature without being damaged and without the occurrence of inflammatory reactions. The sweat glands appear to show some atrophy from disuse on continued exposure to cold. Adaptation is also partly the result of certain habits in that, for example, trained individuals can sleep while shivering, a feat not possible as a rule for the untrained subject. Daniels, Fainer, Bommarito, and Bass (*1232*) 1951 have emphasized from field reports that acclimatization to cold involves the role of many coordinated changes rather than striking changes in any one function. Animal studies of Sellers, Reichman, and Thomas (*1249*) 1951 and Sellers, Reichman, Thomas, and You (*1250*) 1951

have indicated that acclimatized rats show a greatly elevated metabolic rate in comparison with unacclimatized animals. Animals may be artificially acclimatized by pretreatment with a combination of cortisone and thyroxine. The increased rate of survival of the artificially acclimatized rats was not as great as in animals which had acclimatized naturally by previous cold exposure.

A large increase in the ascorbic-acid content has been shown to occur in the tissues of the white rat after prolonged exposure and adaptation to cold (+4° to −4° C.). These studies were carried out by Dugal and Thérien (*1233*) 1947 and Thérien (*1251*) 1949. The increase in ascorbic acid is much smaller if the rats exposed to low temperatures receive daily supplement of that vitamin. On the other hand, a decrease in ascorbic-acid content of the tissues has been found in rats unable to adjust themselves to the cold environment. From these results on the white rat, it appears that acclimatization to low temperatures involves large quantities of ascorbic acid. It is well known that the white rat is able to synthesize ascorbic acid while the guinea pig does not do so. Generally speaking, the tolerance of the guinea pig to cold environment is lower than that of the white rat, and results show that the tolerance of the guinea pig to a cold environment depends on the amount of ascorbic acid received daily. During the process of acclimatization to cold, more ascorbic acid is retained in the tissues of the guinea pig exposed to low temperatures than in the same tissues of control animals kept at room temperature. Finally, a direct relation has been observed by the authors between adaptability to cold environment and the content of ascorbic acid in the adrenal glands. For further studies on ascorbic-acid requirement and acclimatization, a paper by Burton (*1229*) 1949 may be consulted. Butson (*1230*) 1949 found an average increase of 10 mg. percent in the fasting blood-sugar level in men subjected to temperatures of 0° to −35° F. in the Antarctic. There was an increased sensitivity to adrenalin injection as indicated by blood-pressure changes, respiratory rate, pulse rate, and subjective sensations. A greater than normal rise in blood pressure was noted with the cold pressor test.

For a report on acclimatization and the effects of cold on the human body as observed at Little America III, on the United States Antarctic service expedition of 1939 to 1941, a paper by Frazier (*1236*) 1945 may be consulted. Men consistently exposed to low temperatures in this expedition developed dehydration of the skin and subcutaneous structures as a protective measure. The same was observed in other forms of animal life. There is an increase in the blood-sugar levels, and the author states that a vital factor in cold acclimatization is an increase in epinephrine output. For other papers relating to acclimatization and tolerance, reports by the following authors should be consulted: Adolph (*1220*) 1949; Adolph and Molnar (*1223*) 1946; Carlson, Burns, Quinton, and Bark (*1231*) 1949; Gilson (*1238*) 1950; Horvath, Friedman, and Golden (*1241*) 1947; and Irving (*1242*) 1951.

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1253. Anon. Physiologic performance and diet in cold environments. *Nutrit. Rev.,* 1946, *4:* 341–343. [R]

E. EFFECT OF COLD ON EFFICIENCY

Animal experiments of Dureuil and Ratsimamanga (*1254*) 1948 indicate that exposure to sudden temperature drops does not generally alter the work output. Studies on human subjects similarly suggest that men may operate in the cold with unimpaired efficiency with proper protection. Horvath and Freedman (*1256*) 1947 exposed 70 men (50 white and 20 negro) to a temperature environment of −10°, −14°, and −20° F. with zero wind velocity. The subjects wore the 6-piece Arctic assembly with mukluks and felt boots. The handwear was the M–1943 mitten combination. In these studies, the reaction time to visual stimuli was not altered during continuous exposure to a low environmental temperature for periods of 8 to 14 days. Finger dexterity and hand strength were strikingly diminished by exposure to low ambient temperatures, even when the duration of such exposures was relatively short. This loss of hand strength and finger dexterity in cold environments indicates a need for extreme care in the design of equipment for cold-weather operations. Similar conclusions are set forth in a paper by Forlano (*1255*) 1950. Miller (*1257*) 1949 has emphasized that the factor of motivation is highly important in evaluating the efficiency of men doing strenuous work in a cold environment.

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1255. Forlano, G. The effect of ambient and body temperature upon reaction time. *Tech. Data Dig.,* 1950, *15:* 18–24. [R]

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1257. Miller, A. J. Physical fitness for strenuous work in relation to the survival situation in a cold environment. *J. Aviat. Med.,* 1949, *20:* 65–67. [P]

F. IMMERSION IN COLD WATER

In a report on physiological responses to immersion in cold water, Newburgh and Spealman (*1263*) 1943 called attention to the fact that the complete curve of body cooling for the rat seems to be logarithmic in nature. It levels off at a body

temperature a few degrees above the water temperature. The first signs of hypothermia in the rat are drowsiness and motor incoordination which begin to appear as the body temperature falls below 30° C. As it approaches 20° C., unconsciousness supervenes. The initial fall of body temperature of men immersed in cold water progresses in a linear manner. The rate of fall is approximately proportional to the difference between water and body temperature, with a tendency for body temperature to fall more rapidly than expected in the case of lower water temperatures. From experimental evidence gained by the authors, it was inferred that survival time of men immersed in very cold water would be very short. This inference was in agreement with various reports of rapid death of men forced into the cold waters of the North. Immersion in water even as warm as 30° C. (86° F.) was found to cause a considerable fall in body temperature during a 2-hour period of observation. Spealman (*1267*) 1946 found that large dogs do not lose heat in water at 20° C. or above. In water at 15° C. and below, cooling occurs, but some dogs can maintain normal body temperature for at least 5 hours. Dogs become seriously impaired when the rectal temperature declines to about 27° C. In a study of cardiovascular responses of dogs to immersion hypothermia, Hegnauer, Shriber, and Haterius (*1261*) 1950 measured the pulse rate, arterial blood pressure, electrocardiogram, and blood viscosity in relation to temperature within the right heart during immersion hypothermia. In the early stages of hypothermia, the pulse rate reflects the algebraic sum of reflex excitatory and cold depressor influences. In the lower temperature range (25° to 14° C.) the reflex influence seems minimal or absent. The blood-pressure regression with diminishing temperature follows a course independent of the pulse rate until a temperature of 24° to 23° C. is reached, whence complete dependence on pulse rate is evident. The blood viscosity increases twofold to threefold between normal body temperature and 20° C., hemoconcentration accounting in a large measure for the changes. Both systole and isometric relaxation are prolonged progressively with cold, there being a fivefold or sixfold increase at 18° C. It is suggested by the authors that the cause of death in hypothermia is predominantly cardiac, occasioned by inadequate coronary blood flow, on the one hand, and diminished metabolic rate, on the other. The former stems from a fall in pressure head, increased blood viscosity, and prolongation of the tension phases of the cardiac cycle at the expense of the quiescent period. A developing respiratory inadequacy may influence the temperature at which terminal events occur, but does not affect their nature.

For further studies on experimental immersion hypothermia, papers by Penrod (*1264*) 1949 and Wolff and Penrod (*1271*) 1950 should be consulted. In the former paper, it was shown that the oxygen consumption in the dog varied directly with the shivering responses with rectal temperatures above 23° C. Below 23° C. rectal temperature, shivering was no longer a factor and the oxygen consumption of all dogs fell to approximately one-third that of the precooling control level. During rewarming, all dogs shivered greatly when exposed to room air, beginning between 24° and 28° C. rectal temperature. The shivering could be arrested almost at once by immersion in warm water. The oxygen-consumption pattern followed very closely that of the shivering.

There is much evidence, as Spealman (*1269*) 1949 has stated, that hypothermia may rank with asphyxia (drowning) as a cause of death following shipwreck in very cold water. Hence, considerable effort has been expended in devising measures for protecting men in these circumstances. The chief barrier to heat loss from the nude body in cold water is that afforded by the skin and other peripheral tissues. Heat is removed from the nude body more rapidly in cold water than in air at the same temperature. This applied also when ordinary clothing was worn. Minimum water temperatures in which nude men can maintain body temperatures at normal levels is about 32° to 33° C. Most men as well as dogs are chilled fatally in less than 1 hour in water near freezing. Professional distance swimmers use grease for supplying further insulation to their bodies. Large quantities must be applied to be effective, about 18 liters of grease for the average person. In 1945, Spealman (*1266*) supplied data supporting the conclusion that most unprotected men cannot survive long in water below 20° C. One pound of petrolatum spread over the body surface did not afford detectable protection against the cooling action of the cold water. Although 6 pounds afforded some protection, it is not practical in most situations to supply such large quantities of petrolatum for this purpose. Glaser (*1258*) 1950 calculated that in water at 0° to 5° C. the average body temperature of a man would fall by about 0.18° to 0.14° C. per minute and this was confirmed by experiment. A man will withstand a brief immersion at 3° C. without any subjective or objective signs of cooling. Further experiments showed that the heat production of slow swimming was about 230 to 300 calories per square meter of body surface per

hour, and that of moderately fast swimming about 360 calories per square meter of body surface per hour. Such a heat production might roughly equal heat losses in water near the freezing point, and it was concluded that men who are immersed in icy water have a chance of surviving if they can swim or as long as they can swim. This conclusion has been supported by reports of survivors from shipwreck. For a report on survival of men immersed in the ocean, a paper by Molnar (*1262*) 1946 should be consulted. Survival of men in rubber floats after brief immersion in icy water at 4.5° C. has been reported by Glaser and Hervey (*1259*) 1951.

The symptoms of immersion hypothermia are described by Wayburn (*1270*) 1947. In this paper, a report is given of the cases of six patients who suffered from immersion in the North Sea on return from long combat flying missions. Four of the patients showed transient electrocardiographic abnormalities, and one revealed abnormal blood chemical findings. The clinical picture following immersion hypothermia is the resultant of the coldness of the water, the length of exposure, the emotional factors affecting the patient before and during the exposure, and the specific response of the person to cold. The chief effects are those on the cardiovascular system, and among the transient conditions observed were auricular fibrillation and flutter, ventricular extrasystoles, slight prolongation of the P–R interval, and falling of the arterial blood pressure with narrowing of the pulse pressure. The nervous system is also affected, and there may be partial to complete loss of consciousness with irrational behavior. There may be hemoconcentration and notable hyperglycemia. Wayburn recommended rapid restoration of normal body temperature by external heat, minimal activity, administration of warm fluids by mouth, and in severe conditions, use of blood plasma. No drugs were employed in the series reported, and the use of adrenalin was stated to be contraindicated. In a comment on Wayburn's article on immersion hypothermia, Hamburger (*1260*) 1948 discusses the question of rapid rewarming. As a prisoner for 2 years at Buchenwald during World War II, this author stated that he does not consider the so-called experiments at Buchenwald on rewarming to be worthy of serious scientific attention.

For studies of the effects of immersion of the feet in cold water, papers by Spealman (*1265*) 1944 and (*1268*) 1949 should be consulted.

1258. Glaser, E. M. Immersion and survival in cold water. *Nature. Lond.*, 1950, *166:* 1068–1069. [P]

1259. Glaser, E. M. and G. R. Hervey. Survival in rubber floats after brief immersion in icy water. Gt. Brit. MRC–RNPRC. University of Cambridge, Department of experimental medicine. *R. N. P. 51/650, S. S. 38,* April 1951, 5 pp.

1260. Hamburger, R. J. Immersion hypothermia. *Arch. intern. Med.*, 1948, *81:* 109–110.

1261. Hegnauer, A. H., W. J. Shriber, and H. O. Haterius. Cardiovascular response of dog to immersion hypothermia. *Amer. J. Physiol.*, 1950, *161:* 455–465.

1262. Molnar, G. W. Survival of hypothermia by men immersed in the ocean. *J. Amer. med. Ass.*, 1946, *131:* 1046–1050.

1263. Newburgh, L. H. and C. R. Spealman. Physiological responses to immersion in cold water. U. S. NRC–CAM. *C. A. M. rept. no. 164,* 1 August 1943, 10 pp. [P]

1264. Penrod, K. E. Oxygen consumption and cooling rates in immersion hypothermia in the dog. *Amer. J. Physiol.*, 1949, *157:* 436–444.

1265. Spealman, C. R. Early changes occurring in feet exposed to cold water and evaluation of insulation as a means of protection. U. S. Navy. NMRI. *Project X–297: Rept. no. 3,* 17 May 1944, 9 pp.

1266. Spealman, C. R. Body cooling in water and effectiveness of petrolatum in retarding heat loss. U. S. Navy. NMRI. *Project X–189, Rept. no. 4,* 24 May 1945, 9 pp.

1267. Spealman, C. R. Body cooling of rats, rabbits, and dogs following immersion in water, with a few observations on man. *Amer. J. Physiol.*, 1946, *146:* 262–266. [P]

1268. Spealman, C. R. Laboratory and field studies. Wet cold. pp. 367–370 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

1269. Spealman, C. R. Laboratory and field studies. Water. pp. 370–374 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

1270. Wayburn, E. Immersion hypothermia. *Arch. intern. Med.*, 1947, *79:* 77–91. [CH]

1271. Wolff, R. C. and K. E. Penrod. Factors affecting rate of cooling in immersion hypothermia in the dog. *Amer. J. Physiol.*, 1950, *163:* 580–584. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1237. [P]

G. REWARMING AFTER COLD EXPOSURE

For experimental studies on treatment of hypothermia, papers by Hegnauer, Flynn, and D'Amato (*1280*) 1951 and Pichotka and Lewis (*1282*) 1951 should be consulted. In the former report, dogs were subjected to immersion hypothermia and were successfully rewarmed from a mean heart temperature of 16.2° C. (approximately the lethal temperature) when placed in a bath of 45° C. There was return to normal of the pulse rate, blood pressure, P–R and Q–T intervals, and the duration of systole and the isometric relaxation following courses proportional to the increasing cardiac temperature. The relationships on rewarming are almost exactly the reverse of those observed in cooling. This complete reversibility suggested to the authors that, within the temperature limits described, the cardiac phenomena which obtain in cooling represent merely a temperature influence on metabolic rate rather than dysfunction through cardiac pathology. From the ex-

periments reported, there is no evidence that the subendocardial ecchymoses seen at autopsy influence the course of either cooling or rewarming. In the studies by Pichotka and Lewis, it was found that rapid thawing of the frozen legs of rabbits in water at 42° C. for 5 to 8 minutes almost entirely prevented superficial necrosis which generally occurs subsequent to exposures to either −12° C. or −15° C. for 30 minutes. Following the −12° C. exposure, 13 out of 51 rabbits rewarmed in room temperature developed skin necrosis, while none of 75 rapidly thawed animals developed such a complication. Following the −15° C. exposure, 13 out of 33 spontaneously rewarmed rabbits lost their legs and 17 developed superficial necrosis, while only 3 out of 39 rapidly thawed rabbits showed skin injury. Rapid rewarming also was apparently responsible for a decrease in the extent of muscle necrosis, although the difference was sometimes statistically insignificant. Prolonged rewarming in water at 42° C. up to 1 hour produced the same beneficial results as did rewarming for several minutes. Rapid thawing apparently caused severe pain; however, the animals with rapidly rewarmed legs exhibited a better general appearance and preserved better function of the injured limbs than the rabbits whose frozen legs were left to thaw spontaneously.

In a review of work carried out at the Institut fur Luftfahrtmedizin, Munchen, whose director was G. A. Weltz, Alexander (*1272*) pointed out that experimental studies on human subjects had led to a recommendation of the method of rapid and intensive rewarming in a hot water bath at 45° C. for people in shock from exposure to cold, especially in water, in the treatment of service personnel in submarines. It was recommended that the victim should be undressed, immersed in a bath for 10 minutes and then rubbed dry with towels, and placed in heated blankets. If the body temperature does not continue to rise, the hot treatment should be repeated, until the curve of rewarming ascends uniformly by at least 1 degree every 10 minutes. Grosse-Brockhoff (*1277*) 1950 likewise stresses the importance of rapid rewarming in the therapy of hypothermia. To minimize pain, he recommended that rewarming should be started at a water-bath temperature of about 34° C. and increased to approximately 40° to 43° C. within the next 5 to 10 minutes. The quickest possible rewarming is the first precept of this therapy. Medication was believed to play a minor role in acute hypothermia. Atropine had some satisfactory effect by diminishing excessive vagal influences. Even without the presence of hypoglycemia, infusion of glucose solutions had a favorable effect on circulation. In prolonged hypothermia, the primary measure is also rapid rewarming applied in the same way as for acute hypothermia. In the chronic cases, medication is much more important, and large infusions of glucose are stated to be necessary. Cardiac insufficiency is counteracted by strophanthin and atropine is recommended for vagotonia; adrenal extracts are also indicated, according to the author. It is suggested that in all cases of hypothermia, resuscitation by the means of intense heat supply should be attempted as long as the body temperature is not lower than 18° to 20° C. and so long as muscular rigidity still exists. Attempts at resuscitation should not be given up because the state resembles apparent death.

Haterius (*1278*) 1948 investigated the ability of normal dogs to withstand and to recover from cooling of the body. Lightly anesthetized animals were submerged in ice water at about 0° C. until a cardiac or respiratory crisis occurred. Resuscitative measures included rapid rewarming in water at 42° to 45° C. and artificial respiration as required. Thirteen animals survived a reduction in deep rectal temperature to an average of 14.9° C., and recovery was complete in all. The decline in body temperature in cooling was accompanied by a progressive fall in arterial blood pressure and by a bradycardia which became intensified as the temperature of the body fell below 20° C. The slow heart rate was uninfluenced by vagotomy or by atropinization. Eight animals failed to respond favorably or expired before rewarming was begun. In some cases death was due to respiratory failure and in others death was of cardiac origin. These same data are discussed in a paper by Haterius and Maison (*1279*) 1948.

The physiological responses of human subjects to immersion in ice water and to slow and fast rewarming have been the subjects of reports by Behnke and Yaglou (*1275*) 1950 and (*1276*) 1951. In their studies, two nude subjects aged 22 and 46 were immersed shoulder deep in ice water for about 1 hour until the toes became numb. At this point exposure was terminated. The average water temperature varied from about 42° F. in the winter to as high as 50° F. in the summer. Following this drastic chilling, the subjects were rewarmed by exposure to air at 73° F. to 100° F., or to water at 100° F. or to water at 102° F. A third subject dressed in outdoor winter clothing was chilled in a cold chamber at −20° F. for about 3 hours, until his toes became numb. He was then rewarmed in air at 100° F. without changing clothes. Rectal, gastric, and oral temperatures, following initial rise, fell linearly during the cold exposure period. The

conclusive finding in these tests was an abrupt fall of deep body temperatures in a compartively warm environment (air temperature, 73° to 100° F.) following immersion in the iced water or exposure to cold air. In one experiment, the fall of deep body temperature was greater during a period of 20 minutes with the individual in air (73° F.) than it was during the previous 1-hour immersion in cold water (50° F.). There were no untoward effects from the exposures to cold. Reduction or absence of pain after the initial immersion shock, except in the toes, and at the waterline skin areas protruding from the water, was noted. A feeling of intense cold occurred during the initial period of rewarming, despite a high surface temperature. The onset and maintenance of shivering was associated not with the cooling of the skin, but with the fall in deep body temperature. The authors emphasized the need for rapid rewarming of the chilled body to lessen the duration of the precipitous "after drop" of deep temperatures under the conditions of chilling in these experiments.

Ames, Griffith, Goldthwait, Macht, and Belding (*1274*) 1948 have reported a study of various methods of rewarming men after exposure to extreme cold. In these experiments, oxygen consumption, skin temperatures, rectal temperatures, thermal comfort, and onset of shivering of 4 men were determined during 15 experiments, each consisting of a 1-hour exposure to −40° F., followed by 1 hour of rewarming and 1 hour of reexposure to −40° F. Rewarming was attempted by removal of the subject to higher ambient temperature, that is to say, 40° F. or 80° F. A second method consisted of moderate or strenuous exercise; namely, walking on a treadmill at a rate of 2.5 miles per hour on the level or 3.5 miles per hour on a 6.5 percent grade. A third method involved additional thermal insulation (a heavy sleeping bag). A final method consisted of irradiation of the hands or face. The order of efficiency of the various rewarming methods, as measured by change in total body heat, was (1) strenuous exercise, (2) ambient temperature of 90° F., (3) the sleeping bag, (4) ambient temperatures of 40° F., (5) moderate exercise, (6) irradiation of the face, and (7) irradiation of the hands. The first four procedures caused increases in total body heat during the rewarming period, but only in the first was the original heat content approximated. Moderate exercise resulted in cessation of heat loss without gain during rewarming. Irradiation of the hands or face had no significant effect on the total heat content. In all cases, the body heat decreased during the second hour of cold exposure at approximately the same rate as during the first hour. The only indications of acclimatization, based on results of control experiments, were a progressive increase in thermal comfort and a progressive delay in the onset of shivering during successive exposures. Commenting upon these same experiments, Ames, Goldthwait, Griffith, and Macht (*1273*) 1948 reported that the ingestion of glucose had little effect on the reactions of men to cold. It slightly delayed the fall in internal temperature. Under the conditions of this investigation, taking alcohol did not cause significant peripheral vasodilatation in men who had been exposed to cold. It delayed the fall in internal temperature and increased thermal comfort. In qualification of this finding, it should be pointed out that there is good evidence that alcohol lowers resistance to cold. The repeated short periods of cold exposure used in this series of experiments did not produce evidence of acclimatization in terms of cooling curves. The subjects appeared to maintain thermal comfort longer as the experiment progressed, and the time elapsed before the onset of shivering was extended. For further studies on therapy after exposure to cold, three additional reports may be consulted (*1281, 1283,* and *1284*).

1272. Alexander, L. The treatment of shock from prolonged exposure to cold especially in water. U. S. Army. Combined intelligence objectives subcommittee, APO 413, Allied forces. *C. I. O. S. Target No. 24.* 221 pages.

1273. Ames, A., D. A. Goldthwait, R. S. Griffith, and M. B. Macht. An evaluation of methods of rewarming men. Including a brief investigation of the effects of glucose, alcohol and successive exposures on the reactions of men to cold. U. S. Army. Office of the Quartermaster General, Lawrence, Mass. Quartermaster climatic research laboratory. Environmental protection section, *Rept. no. 134,* 31 August 1948, 40 pp.

1274. Ames, A., R. S. Griffith, D. A. Goldthwait, M. B. Macht, and H. S. Belding. A study of various methods of rewarming men after exposure to extreme cold. *Fed. Proc. Amer. Soc. exp. Biol.,* 1948, *7:* 2–3.

1275. Behnke, A. R. and C. P. Yaglou. Responses of human subjects to immersion in ice water and to slow and fast rewarming. U. S. Navy. NMRI. *Project X–189, Rept. no. 11,* 23 March 1950, 16 pp. *XVIII Intern. physiol. Congr.,* August 15, 1950, 98–99.

1276. Behnke, A. R. and C. P. Yaglou. Physiological responses of men to chilling in ice water and to slow and fast rewarming. *J. appl. Physiol.,* 1951, *3:* 591–602.

1277. Grosse-Brockhoff, F. Pathologic physiology and therapy of hypothermia. Therapy of acute hypothermia. pp. 839–842 in: *German aviation medicine. World War II. Vol. II.* Department of the Air Force, Washington, D. C., 1950, 1302 pp. [R]

1278. Haterius, H. O. Experimental hypothermia and rewarming in the dog: recovery after severe reduction in body temperature. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Tech. rept. no. MCREXD–696–113,* 5 February 1948, 23 pp. [P]

1279. Haterius, H. O. and G. L. Maison. Experimental hypothermia and rewarming in the dog: recovery after

severe reduction in body temperature. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command, ENG. Aero medical laboratory. *Serial no. MCREXD–696–113,* 5 February 1948, 23 pp. *Amer. J. Physiol.,* 1948, *152:* 225–232. [P]

1280. Hegnauer, A. H., J. Flynn, and H. D'Amato. Cardiac physiology in dog during rewarming from deep hypothermia. *Amer. J. Physiol.,* 1951, *167:* 69–75. [P]

1281. Jaulmes ( ) and ( ) Benitte. Traitment de l'hypothermie. *Méd. aeronaut.,* 1950, *5:* 73–74.

1282. Pichotka, J. and R. B. Lewis. Effect of rapid and prolonged rewarming on the extent of local cold injury. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–006, Rept. no. 7,* April 1951, 14 pp. *Armed Forces med. J.,* 1951, *2:* 1293–1310.

1283. Smith, S. Treatment of conditions arising from exposure to extreme cold. pp. 4–400—4–410 in: *Treatment in general medicine.* Volume 4. Edited by Hobart A. Reimann. Fourth edition. Philadelphia, F. A. Davis Co., 1948, 776 pp.

1284. Anon. Therapy after exposure to cold. *Air-sea rescue bulletin.* 1946, *3:* 22–23.

H. PATHOLOGICAL EFFECTS OF COLD

In a report on the epidemiology of trauma, Whayne (*1301*) 1950 has stressed the importance of trenchfoot and, to a less extent, frostbite as components of nonbattle trauma. In World War II, the average disability period per case was in excess of 50 days, and only between 10 and 20 percent of cases, serious enough to receive hospital care, ultimately could be returned to full combat duty. The pathological process of cold injury has been compared with that of thermal burns, except that coagulation of serum components does not occur. Talbott (*1298*) 1950 has pointed out that trenchfoot occurs in wet environments with the air temperature near freezing. Immersion foot occurs usually at sea, on liferafts, and so forth, where temperatures may be higher. Heat loss is accelerated by a moist environment because wet clothing has very little insulative value. The early symptoms are numbness, tenderness, and muscle cramps, preceded by pain. Exposures of not more than 12 hours may be sufficient to produce immersion foot. Pulsations are absent in the peripheral arteries. There is loss of cutaneous sensation and the skin is pale and waxy white. When the victim is moved to a warm environment, the affected member develops a bright red flush and arterial pulsations become clear and bounding. There is rapid swelling and the foot becomes hot and dry. Blisters, ecchymoses, and areas of gangrene may appear. A patient is restless, toxic, and in need of sedation. Talbott recommends that the limbs be elevated but not rubbed. Asepsis must be maintained and antibiotics are recommended. The feet should be exposed to moderately cool air (20° C.). Frostbite is a hazard at subzero temperatures (about −10° C. and below) with high winds. Inspection shows pearly white areas surrounded by pale-pink skin. The white area becomes suffused and red on return to warm environment. Tingling and paresthesia may persist for 1 or 2 days, and the affected area may desquamate. The parts should not be rubbed, and antibiotics should be administered judiciously.

The development of tissue damage due to cold has been reported and discussed by Kreyberg (*1288*) 1946. As the skin is chilled, the initial changes are purely physiological adjustments to cold. At first, the blood vessels contract and the skin is cold and cyanotic. The skin then becomes very red with a high oxygen content, since metabolic processes are greatly slowed. Also there is a shift to the left in the oxyhemoglobin dissociation curve. The skin becomes numb and the extremities clumsy. Below 10° C., the skin is pink and there is pain with successive waves of blood-vessel constriction and dilation. Following this, where the temperature has fallen well below 0° C., actual freezing of the tissues occurs. Three types of cold exposure may be distinguished: (1) Short exposure to moderate cold with return to normal, (2) freezing the tissues to ice and return to normal temperature, and (3) long exposure to moderate cold with a return to normal temperature. In all of these, the pathological reaction to cold is an acute aseptic inflammation which produces hyperemia, edema, and necrosis. The necrosis is believed to result from blood stasis following loss of plasma through the very permeable capillary wall. In the treatment of tissue damage due to cold, rapid heating and rubbing are to be avoided. The author recommends that the limb be elevated and gradually rewarmed to normal temperatures. Kreyberg (*1289*) 1949 found that heparin did not influence the development of stasis, and considered that heparinization is of little value in the prevention of necrosis after freezing. Increased permeability was considered the important element in the development of stasis.

Friedman (*1286*) 1946 has stated that there is no essential dissimilarity between the lesions of trenchfoot and of high-altitude frostbite. He believes that agglutinative thrombosis resulting in ischemic gangrene can account for the most severe lesions. Essex and Quintanilla (*1285*) 1946 have investigated experimentally the question of whether frostbite results in coagulation of the blood in the smaller vessels leading to anoxia and further destruction of the frostbitten tissue. In his study, use was made of the Florey modification of the Clark transparent chamber inserted into the ears of rabbits. Pieces of carbon dioxide ice were applied

directly to the window for 30 seconds. The vessels that had grown into the chamber were completely frozen. Immediately after thawing, the vessels appeared normal in all respects. However, after 5 or 10 minutes, it was apparent that serious injury had been done. The vessels became widely dilated and filled with red and white blood cells. The permeability of the vessel walls was increased and the plasma was drained from the vessels, leaving the formed elements concentrated in the vessels in conglomerate masses. Coagulation was not a factor since an identical picture was seen in the vessels of animals whose blood had been rendered incoagulable by injections of heparin. For a Russian report on the pathogenesis of frostbite, a paper by Piontkovskii (*1296*) 1949 may be consulted. This author states that the majority of the Soviet research workers recognize that one of the leading causes of frostbite seems to be tissue asphyxia. In the author's experiments, chilling of isolated tissue reduced oxidative and glycolytic processes significantly. The damage to the tissue respiratory system was reversible or irreversible, depending upon the degree and duration of chilling. It was found that the respiratory mechanism of the epidermal tissues was more resistant to chilling than that of muscular tissue.

Regarding the treatment of frostbite, Lane and Bolleruf (*1290*) 1951 dressed all breaks in the skin or anticipated breaks with loose sterile vaseline dressings. Cases with open lesions were given penicillin. Whirlpool baths were administered to the majority of cases without open lesions. A very few cases required surgical intervention, the times between exposure to cold and amputation being 58 to 86 days. The authors stated that early surgery in frostbite cases seems contraindicated because of the possibility that such premature surgery might remove tissue which would eventually survive. To determine whether cortisone is effective in decreasing the extent of necrosis resulting from standardized local cold injuries, Lewis and Freytag (*1293*) 1951 subjected rabbits to local cold injury for 7 days with or without treatment with 5 mgs. of cortisone intramuscularly each day for 2 days beginning with the day of exposure followed by 3 mgs. a day for 4 days. There was no significant difference between the cortisone treated and control animals in the extent of skin necrosis or muscle necrosis. Lewis (*1292*) 1951 has likewise determined the effect of rapid thawing of frostbitten rabbit legs with shortwave diathermy on the extent of skin and muscle necrosis. In these studies, it was found that the use of short wave diathermy did result in a decrease in the extent of muscle and skin necrosis in comparison with control frostbitten animals thawed at room temperature in air. Pichotka, Lewis, and Luft (*1295*) 1950 found that hypoxia did not influence the extent of necrosis due to local cold injury if present only during the exposure to cold and in a preparatory period up to 30 minutes. Hypoxia after local cold injury increased the extent of the resulting damage as measured by the proportion of necrotic tissue in the exposed leg. The increase was in direct relationship to the length of the period of hypoxia. It is conceivable, according to the authors, that general hypoxia induces this effect by local oxygen deficiency or by impairment of the peripheral circulation. Hypoxia preceding cold injury influenced the outcome in a complicated manner. Cases with a preparatory hypoxia period up to 60 minutes were not different in their results from controls exposed to cold injury alone. Slightly longer hypoxic periods (60 to 90 minutes or 60 to 120 minutes) resulted in a striking increase in the extent of injury measured as proportion of necrotic muscle tissues and as extent of the superficial skin necrosis. A further prolongation of the preceding hypoxic period (120 to 180 minutes) brought the extent of injury back to that of the controls and, finally, with a duration of 180 to 300 minutes, the extent of injury was below that of the controls. The authors attribute the differences in extent of necrosis observed after different lengths of the hypoxic period prior to cold injury to factors secondary to general hypoxia. According to Pichotka, Lewis, and Freytag (*1294*) 1951, functional and anatomical changes in rabbit legs show a sequence of increasing local injury in proportion to the degree of cold. Exposure to 5° C., 0° C., and −5° C. for 30 minutes resulted in temporary functional changes. The abnormalities noted were loss of muscular power in the leg and foot, absence of response or hyperactive reaction to pinprick, loss of the spreading reflex of the toes, and, in some cases, hyperextension of the ankle joint. Muscle atrophy was observed in the more severe of these exposures and represented extension into a second category of increasing injury. This second category included those animals exposed for 30 minutes to −10° C. to −12° C. In these animals there was, in addition to the functional changes described for the first category, also isolated necrosis of muscle. In the third category, those animals exposed to temperatures below −12° C. for 30 minutes, there was skin necrosis in addition to the abnormalities observed in the first and second categories. Often, the end result of these severe injuries was complete loss of the leg.

For further reports on the pathological effects of cold, papers by the following may be consulted:

Hegnauer and Penrod (*1287*) 1949; Lange, Weiner, and Gold (*1291*) 1949; Sawatari (*1297*) 1950; and U. S. Navy (*1299, 1300*) 1948.

1285. Essex, H. E. and R. Quintanilla. Effects of frostbite on the minute blood vessels of a peripheral vascular bed. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 25–26.

1286. Friedman, N. B. The reactions of tissue to cold. The pathology of frostbite, high altitude frostbite, trench foot and immersion foot. *Amer. J. clin. Path.*, 1946, *16:* 634–639.

1287. Hegnauer, A. H. and K. E. Penrod. Observations on the pathologic-physiology in the hypothermic dog. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Technical rept. no. 5912,* August 1949, 108 pp. vi.

1288. Kreyberg, L. Tissue damage due to cold. *J. industr. Hyg.*, 1946, *28:* abstract section: 83. *Lancet,* 1946, *1:* 338–340.

1289. Kreyberg, L. Development of acute tissue damage due to cold. *Physiol. Rev.*, 1949, *29:* 156–167. [R, D]

1290. Lane, F. H. and F. Bolleruf. Evaluation of methods for the treatment of frostbite. USAF. Ladd air force base, Alaska. Arctic aeromedical laboratory, *Project 21–01–012,* January 1951, 14 pp.

1291. Lange, K., D. Weiner, and M. A. Gold. Studies on the mechanism of cardiac injury in experimental hypothermia. *Ann. intern. Med,* 1949, *31:* 989–1002. [P]

1292. Lewis, R. B. Microwave diathermy treatment of frostbite. USAF. Randolph Field, Texas. School of aviation medicine. *Project 21–23–006, Rept. no. 11,* August 1951, 3 pp.

1293. Lewis, R. B. and E. Freytag. Use of cortisone in the treatment of experimental frostbite. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–006, Rept. no. 9,* August 1951, 3 pp. [P]

1294. Pichotka, J., R. B. Lewis, and E. Freytag. Sequence of increasing local cold injury. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–006, Rept. no. 6,* March 1951, 16 pp.

1295. Pichotka, J., R. B. Lewis, and U. C. Luft. The influence of general hypoxia on local cold injury. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–016, Rept. no. 2,* July 1950, 8 pp. [P]

1296. Piontkovskii, I. A. K voprosy o proiskhozhdenii tkanevoi asfiksii pri otmorozheniiakh. [Contributions to the etiology of tissue asphyxia in frostbite.] pp. 246–251 in: *Gipoksiia,* Kiev, Akad. Nauk Ukr. SSR., 1949, 415 pp.

1297. Sawatari, J. Influence of atmospheric cold upon ear, nose, throat, and their diseases. *J. oto-rhinolaryng. Soc., Tokyo,* 1950, *53* (*12*)*:* 428–435. (Japanese text pagination.) (English text pagination.) 53–54.

1298. Talbott, J. H. Cold: pathologic effects. pp. 252–255 in: *Medical physics. Volume II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

1299. U. S. Navy. Office of Naval Advisor, Office of Military Government for Germany, Medical Section. Effect of Cold. pp. 51–66 in: *Report of the second conference of special medical consultants from 30 November to 3 December 1942 at the Military Medical Academy, Berlin.* Project 1, Folio VII, 23 March 1948, 137 pp.

1300. U. S. Navy. Office of Naval Advisor, Office of Military Government for Germany, Medical Section. Injuries due to cold. pp. 164–188 in: *Report of the second conference of special medical consultants from 30 November to 3 December 1942 at the Military Medical Academy, Berlin.* Project 1, Folio VIII, 23 March 1948, 226 pp.

1301. Whayne, T. F. *Cold injury in World War II. A study in the epidemiology of trauma.* Thesis, (Med.), Harvard School of Public Health. Boston, Mass., 1 May 1950, 364 pp.

VII. VISUAL PROBLEMS

A. GENERAL CONSIDERATIONS

United States submarine medical activities have continued to play a significant role in visual research. For a review of this work, a report by Shilling (*1306*) 1951 should be consulted. Laboratory research in vision is carried out at the U. S. Submarine Base, New London, Conn., and at the U. S. Naval School of Aviation, Pensacola, Fla., with field studies at Camp Lejeune and at the Naval Medical Research Institute, Bethesda. University laboratories and research institutes are also engaged in visual research in coordination with the U. S. Navy. A general introduction into the military visual problems is provided the reader in the general references that follow as well as in the references under specific headings below. The reader is particularly advised to consult the papers by Harris (*1304*) 1948 and Miles and Bronk (*1305*) 1948.

1302. Chapanis, A. How we see: a summary of basic principles. pp. 3–60 in: *A survey report on human factors in undersea warfare,* Washington, D. C., National Research Council, 1949, 541 pp.

1303. Chapanis, A., W. R. Garner, and C. T. Morgan. How we see. Basic problems of visibility. pp. 76–93 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

1304. Harris, J. D. Some relations between vision and audition. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 000–009, Rept. no. 1,* 21 July 1948, 22 pp. [R]

1305. Miles, W. R., and D. W. Bronk. Visual problems. pp. 261–277 in: Part III. Aviation Medicine in: *Advances in Military Medicine, Vol. I.* Edited by E. C. Andrus, D. W. Bronk, G. A. Carden, Jr., C. S. Keefer, J. S. Lockwood, J. T. Wearn, and M. C. Winternitz. Boston, Little, Brown and Co., 1948, 472 pp. [R]

1306. Shilling, C. W. Visual research in the U. S. Navy. *Trans. Amer. Acad. Ophthal. Oto-laryng.*, 1951, *56:* 868–871.

1307. Streltsov, V. The function of the eye in aviation. *Amer. Rev. Soviet Med.*, 1944, *2:* 126–133.

1308. Talbot, S. A. Vision. *Annu. Rev. Physiol.*, 1949, *11:* 245–268. [R]

B. ACUITY

A number of studies on the measurement of visual acuity have been reported from the U. S. Submarine Base, New London, Conn. In 1945, Sulzman, Farnsworth, Cook, Bartlett, and Kindred (*1326*) reported a comparison of various screening devices with standard medical visual procedures. This re-

port gave results of work done to determine the validity and reliability of various visual screening devices including the Ortho-Rater. It was evident to the authors that clinical visual testing procedures were not sufficiently standardized to permit comparisons of the performance of the various devices. In 1946, Sulzman, Cook, and Bartlett (*1325*) investigated the comparative efficiencies of the Keystone Telebinocular, the Bausch and Lomb Ortho-Rater, and the American Optical Sight Screener. Of the three, the Telebinocular proved inferior in both validity and reliability to the Ortho-Rater and the Sight Screener with no choice indicated between the latter two. In every instance the reliability of measures of acuity for distance was found to be greater than the reliability of measures for near vision. Reliability of measurements with screening instruments was found to be inferior to that of letter-chart tests conducted according to standard methods. Suggestions were made by the author for improvement of the Snellen charts. Similar results are given by Cook (*1311* and *1312*) 1948. Dimmick and Rudolph (*1313*) 1948 have examined checkerboard visual acuity targets of various sizes to determine whether they contain secondary cues which could distort visual acuity measurements taken with them. A series of valid targets have been obtained. Such a series is an essential element in a program of visual-acuity measurement. Dimmick and Rudolph (*1314*) 1948 and Pratt and Dimmick (*1322*) 1951 have reported ophthalmological studies of visual acuity under dim illumination.

For other studies on visual acuity, the reference list below may be consulted.

1309. Beyne, P. J. E. La mesure correcte de l'acuité visuelle chez l'homme. *Méd. aeronaut.*, 1950, *5:* 3–18.

1310. Chapanis, A. Vision. *Annu. Rev. Physiol.*, 1948, *10:* 133–156. [R]

1311. Cook, E. B. Visual acuity measurements with three commercial screening devices. U. S. Navy. Submarine base, New London, Conn. Medical research department, (A revision of progress report No. 2 of BuMed research. *Project no. X–493* (*Av–263–p*) by Sulzman, Cook and Bartlett, 7 February 1946), 22 April 1948, 44 pp. [P]

1312. Cook, E. B. Comparative performance of commercial screening devices and far and near wall charts utilizing the same test targets. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM–003–011* (*X–493*), *Rept. no. 5,* 30 August 1948, 56 pp. [P]

1313. Dimmick, F. L. and L. M. Rudolph. Checkerboard visual acuity targets: an experimental validation. U. S. Navy, Submarine base, New London, Conn. Medical research laboratory. *Project NM–003–008* (*X–423*), *Rept. no. 1,* December 1948, 14 pp.

1314. Dimmick, F. L. and L. M. Rudolph. Variations in visual acuity under different conditions of illumination. U. S. Navy. Submarine base, New London, Conn. Medical research department, *Project NM–003–008* (*X–423*), *Rept. no. 1,* December 1948, 14 pp.

1315. Feinberg, R. and S. E. Wirt. Visual acuity in relation to illumination in the Ortho-Rater. *J. appl. Psychol.,* 1947, *31:* 406–412.

1316. Giese, W. J. The interrelationship of visual acuity at different distances. *J. appl. Psychol.,* 1946, *30:* 91–106. [P]

1317. Junes, ( ). Acuité visuelle et service militaire. *Arch. Ophtal., Paris,* 1951, *11:* 358–369.

1318. Kuntz, J. E. and R. B. Sleight. Effect of target brightness on "normal" and "subnormal" visual acuity. *J. appl. Psychol.,* 1949, *33:* 83–91. [P]

1319. Low, F. N. Studies and investigations in connection with a test for peripheral visual acuity; the development of simple form acuity in the retinal periphery during dark adaptation under scotopic conditions. U. S. NRC–CAM. *OEMcmr–345, C. A. M. rept. no. 464,* 7 June 1945, 24 pp.

1320. Low, F. N. The peripheral motion acuity of 50 subjects. *Amer. J. Physiol.,* 1947, *148:* 124–133.

1321. Mandelbaum, J. and L. L. Sloan. Peripheral visual acuity, with special reference to scotopic illumination. *Amer. J. Ophthal.,* 1947, *30:* 581–588. [P]

1322. Pratt, C. and F. L. Dimmick. An ophthalmological study of visual acuity under dim illumination. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 003 041.04.04, Rept. no. 173,* 6 June 1951, 15 pp.

1323. Rose, H. W. Visual acuity and refraction. Effect of vibration on visual acuity. pp. 891–892 in: *German aviation medicine World War II. Vol. II.* Department of the Air Force, Washington, D. C., 1950, 1302 pp.

1324. Senders, V. L. The physiological basis of visual acuity. *Psychol. Bull.,* 1948, *45:* 465–490.

1325. Sulzman, J. H., E. B. Cook, and N. R. Bartlett. Visual acuity measurements with three commercial screening devices. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–493* (*Av–263–p*), *Rept. no. 2,* 7 February 1946, 43 pp.

1326. Sulzman, J. H., D. Farnsworth, E. B. Cook, N. R. Bartlett, and M. I. Kindred. Comparison of various screening devices with standard medical visual procedure. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–493* (*Av–263–p*), *Rept. no. 1,* 23 November 1945, 50 pp.

1327. Tufts College. Visual acuity. 12 pp. in: *Handbook of human engineering data for design engineers.* Tufts College, Institute for applied experimental psychology. *SDC Human Engineering Project 20–G–1, Project Designation NR–783–001, Technical Report 199–1–1,* 1 December 1949, 410 pp.

1328. U. S. Army. Staff, Personnel research section, Adjutant General's office. Studies in visual acuity. *Rept. no. 742.* Washington, D. C., U. S. Government Printing Office, 1948, 161 pp. [P]

1329. Warden, C. J. An investigation of motion acuity under scotopic conditions at various retinal positions. U. S. NRC–CAM. *C. A. M. rept. no. 182,* 6 August 1943, 17 pp. [P]

1330. Warden, C. J. An investigation of motion acuity under scotopic conditions at various retinal positions. U. S. NRC–CAM. *OEMcmr–264, C. A. M. rept. no. 477,* 20 October 1945, 23 pp. [P]

1331. Warden, C. J. and H. C. Brown. A preliminary investigation of form and motion acuity at low levels of illumination. *J. exp. Psychol.*, 1944, *34:* 437–449.

C. COLOR VISION

For United State naval research on color vision conducted chiefly at the U. S. Submarine Base, New London, Conn., the following references should be consulted: *1333, 1335, 1336, 1337, 1338, 1339, 1340, 1341, 1348, 1351, 1353, 1356,* and *1357.* Farnsworth (*1336*) 1950 has pointed out that no hope for improvement of defective color vision can be expected from any treatment although education tends to improve somewhat the color discrimination of both normal and color defective individuals. Assignment of personnel in any kind of job should be preceded by an understanding of the degree of color perception required in positions to be filled. Farnsworth (*1335*) 1946 reported the development and trial of the New London navy lantern as a selection test for serviceable color vision. It was concluded that the new model lantern seems to represent the most effective instrument for testing color vision of naval personnel. The New London navy lantern color-vision test has been evaluated by Rand and Ray (*1351*) 1950. On the basis of analysis of results for various conditions, the authors concluded that to enjoy maximum test-retest reliability, the New London test must be employed under conditions for which it was designed. Several possibilities for improving the New London test were considered. Studies of the pseudo-isochromatic plates for color-vision testing have been carried out by Farnsworth (*1337*) 1951, Farnsworth and Reed (*1338*) 1944 and (*1339*) 1945. A preliminary report on color vision is given by Shilling (*1356*) 1942. This author (*1357*) 1943 has also reported tests of the Royal Canadian Navy color-vision lantern in comparison with other tests of color vision.

Farnsworth and Reed (*1340*) 1946 have reported on comparative reaction times to "Christmas tree" signal lights with respect to color deficiency. One of the most important color discriminations involved in the operation of a submarine is that of reading the "Christmas tree," a panel of 30 to 60 small jewel-shaped lights, used to indicate whether hull openings, such as hatches and vents, are sealed or not. Electrical connections with the various openings cause the indicator board to light up. Each hatch controls a pair of lights on the board. If a hatch is open, the red member of this pair is lighted; if it is closed, the green light comes on. When the board is entirely green, the submarine is rigged for diving. Diving operations are performed with split-second timing, and in these moments the safety of the submarine depends upon the appearance of the "Christmas tree." Since the colored lights are a vivid red and clear green, it may be assumed that all colorblind individuals except extreme cases could distinguish between the colors. However, it has been assumed that colorblind individuals would be slower or less accurate in making such discriminations than men with normal color vision. The authors have attempted to check the accuracy of these assumptions. The "Christmas tree" was wired so that the observers' reaction times to the red and green light signals could be measured. A group of 4 colorblind subjects was compared with a group of 6 color-normal individuals to determine the difference in mean reaction times when lights were at full brightness. Four hundred and sixty trials were given each man. Slight difference was found between the two groups. Since on patrol the lamps are customarily burned on reduced voltage, tests were carried out to approximate the appearance of a dimmed board. To accomplish this, the green jewel was changed slightly in color by the addition of a yellow filter. Two colorblind subjects and two men with normal-color vision were tested under these conditions. The change in color greatly lengthened the reaction time of the colorblind subjects but not of the normal subjects. It was concluded from the experiments that colorblind individuals are able to read the "Christmas tree" at full brightness nearly as rapidly as normal subjects. As the voltage supplying the lamps in the "Christmas tree" is dropped, the colorblind subjects may be expected to show progressively greater hesitancy in discriminating the red from the green jewels. The use of bluish-green glasses would be expected to decrease the confusion effect for colorblind subjects.

For other studies on color vision and color-vision testing, the references given below should be consulted.

1332. Christian, P., R. Haas, and V. V. Weizsacker. Über ein Farbenphänomen. (Polyphäne Farben.) *Pflüg. Arch. ges. Physiol.*, 1948, *249:* 655–701. [D] [P]

1333. Farnsworth, D. The effect of colored lenses upon color discrimination. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Color vision rept. no. 9, N. L. Sub.–1–CV–17, Project X–502* (*Av–269–p*), 3 September 1945, 15 pp.

1334. Farnsworth, D. and P. Foreman. A brief history of lanterns for testing color sensation and description of the essential principles. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–457* (*Av–241–k*), *Preliminary Rept.*, 15 April 1946, 12 pp.

1335. Farnsworth, D. Development and trial of New London navy lantern as a selection test for serviceable color vision. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–457* (*Av–241–k*), *Final Rept.*, 6 May 1946, 39 pp. [P]

1336. Farnsworth, D. Color vision. pp. 309–311 in: *Handbook of applied psychology.* Volume 1. Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart and Co., Inc., 1950, ix, 380 pp.

1337. Farnsworth, D. Proposed armed forces color vision test for screening. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.10.01,* 20 August 1951, 9 pp.

1338. Farnsworth D. and J. D. Reed. The effect of changing the illumination on the colors in pseudo-isochromatic plates. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Color Vision Rept. no. 5,* 3 January 1944, 10 pp.

1339. Farnsworth, D. and J. D. Reed. Comparison and evaluation of American Optical Co. pseudo-isochromatic plates, first and second editions. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–480 (Av–255–p), Rept. no. 8,* 19 March 1945, 50 pp.

1340. Farnsworth, D. and J. D. Reed. Comparative reaction times to Christmas tree signal lights with respect to color deficiency. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–265 (Av–153–c), Rept. no. 10,* 5 February 1946, 11 pp.

1341. Farnsworth, D., J. D. Reed, and C. W. Shilling. The effect of certain illuminants on scores made on pseudo-isochromatic tests. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Color vision rept. no. 4,* 22 November 1943, reissued 1 December 1948, 9 pp.

1342. Frick, D. C., E. L. Green, and J. M. Fry. The AAF. SAM color code test (Colcode); a performance test of color discrimination ability. USAF. Randolph Field, Tex. School of aviation medicine, *Project 415, Rept. no. 1,* 18 September 1945, 15 pp.

1343. Granit, R. A physiological theory of colour perception. *Nature, Lond.,* 1943, *151:* 11–14.

1344. Hardy, L., G. Rand, and C. Rittler. Les épreuves de la vision des couleurs. *Ann. Oculist., Paris,* 1950, *183:* 515–518. [D]

1345. Hardy, L., G. Rand, and C. Rittler. La vision des couleurs et les travaux recents sur les épreuves de la vision colorée. *Ann. Oculist., Paris,* 1950, *183:* 519–532. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1298.

1346. Hartridge, H. A proposed colour blindness test. *Proc. ninth intern. Congr. industr. Med., London,* 1948, 1052–1053. (French summary.)

1347. Hartridge, H. Human colour vision. *XVI Concil. ophth. 1950 Acta, 1:* 561–567. (French and Spanish summaries.)

1348. Malone, F. L., M. S. Sexton, and D. Farnsworth. The detectability of yellows, yellow-reds, and reds, in air-sea rescue. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.35.01,* 27 September 1951, 8 pp.

1349. Motokawa, K. A physiological basis of color discrimination. *Tôhoku J. exp. Med.,* 1949, *51:* 197–205. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1257. [P]

1350. Peckham, R. H. The influence of sun glasses on object-color perception. Temple University, Philadelphia. *O. N. R. contract no. NR 142–565,* 16 September 1949. 28 pp. [P]

1351. Rand, G. W. and J. T. Ray. Evaluation of the New London Navy lantern color vision test. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. Joint report with Tulane University, Department of psychology. *Report no. 1,* 16 May 1950, 17 pp. [P]

1352. Rose, H. W. and I. Schmidt. Physiological effects of reflective, colored, and polarizing ophthalmic filters. II. Effect of ophthalmic filters on color vision. USAF, Randolph Field, Tex. School of aviation medicine. 2nd printing to replace issue distributed November 1949. *Project 21–02–040, Rept. no. 2,* March 1950, 29 pp. [P]

1353. Schelling, H., von. A method for calculating the effect of filters on color vision. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 000 009, Rept. no. 3,* 15 September 1949, 14 pp. [P]

1354. Schmidt, I. New tests for the examination and training of color vision. 1. Pseudo-isochromatic plates. USAF. Randolph Field, Tex. School of aviation medicine. *Project 517, Rept. no. 1,* July 1948, 11 pp. [P]

1355. Schmidt, I. Comparative evaluation of the New London Navy lantern for testing color perception. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–29–009,* August 1951, 10 pp.

1356. Shilling, C. W. Preliminary report on color vision testing. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–42 (V5–2),* September 12, 1942, 14 pp.

1357. Shilling, C. W. Royal Canadian Navy colour vision lantern in comparison with other tests of color vision. U. S. Navy. Submarine base, New London, Conn. Medical research division. *Project X–42 (Av–5–2),* 18 January 1943, 21 pp.

1358. Willmer, E. N. *Retinal structure and colour vision. A restatement and a hypothesis.* Cambridge, The University Press, 1946, 231 pp.

1359. Wright, W. D. *Researches on normal and defective colour vision.* London, Henry Kimpton, 1946, 383 pp.

D. VISUAL PERFORMANCE

For United States naval studies on practical problems concerned with visual performance, the following references should be consulted: *1363, 1364, 1371, 1373, 1374,* and *1375.* In 1948, Farnsworth (*1363*) reported proposed modifications of red and green navy signal lights. Standards for general-purpose sunglasses were given by Farnsworth (*1364*) in 1948. Sperling and Farnsworth (*1371*) 1950 have discussed factors determining periscope acuity at night.

A highly important task in the submarine is the reading of the dials of the TDC. Verplanck (*1373*) 1946 has reported an experiment on the legibility of the TDC under several conditions of illumination and adaptation. Two measures of efficiency in reading the dials of the TDC were obtained on six subjects, under several conditions of preadaptation and of conning-tower illumination. In both measures of efficiency, changes associated with the preadaptation conditions were observable. Subjects who had previously adapted in red illumination for 15 minutes read the TDC dials more quickly and with fewer errors than when they were not pre-

adapted. For a comprehensive discussion of visual communication, a report by Verplanck (*1375*) 1949 should be consulted.

Other studies on visual performance are reported in the references given below.

1360. Bartley, S. H. The basis of visual fatigue. *Amer. J. Optom.*, 1947, *24:* 372–384.

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1363. Farnsworth, D. Proposed specifications of red and green navy signal lights. U. S. Navy, Submarine base, New London, Conn. Medical research department. *Project X–265 (Av–153–c), Adjunct Rept.*, 1 March 1948, 17 pp.

1364. Farnsworth, D. Standards for general purpose sunglasses. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 000 009, Rept. no. 2,* 10 September 1948, 27 pp.

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1366. Kravkov, S. V. Stimulating visual function. *Amer. Rev. Soviet Med.*, 1944–45, *2:* 353–355.

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1368. Saunders, E. E. Navy eye-correction, eye-protection program. *Trans. Amer. Acad. Ophthal. Oto-laryng.*, 1947–48, *52:* 562–565.

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1372. Stump, N. F. Industrial safety and visual functions. *J. Psychol.*, 1945, *20:* 369–379.

1373. Verplanck, W. S. A brief experiment on the legibility of the TDC under several conditions of illumination and adaptation. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–519 (Av–273–p), Final Rept.*, 15 March 1946, 8 pp.

1374. Verplanck, W. S. A field test of the use of filters in penetrating haze. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM–011–003, Final Rept.*, 6 June 1947, 11 pp. [P]

1375. Verplanck, W. S. Visual communication. pp. 249–266 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

1376. Williams, S. B. Visibility on cathode-ray tube screens: viewing angle. *J. opt. Soc. Amer.*, 1949, *39:* 782–785. [P]

1377. Williams, S. B. Visibility on radar scopes. pp. 101–130 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

E. ACCOMMODATION

The status of this subject from the point of view of the submarine service remains virtually the same as at the time of preparation of the first volume of this Sourcebook.

1378. Peterson, J. H. and E. Simonson. Effect of glare on accommodation near point. *Amer. J. Ophthal.*, 1951, *34:* 1088–1092. [P]

F. PHORIA

Cook (*1379*) 1948 has reported a factor analysis of acuity and phoria measurements obtained with commercial screening devices and by standard clinical methods. A comparative study of measures of heterophoria has been reported by Sulzman, Cook, and Bartlett (*1381*) 1946. Both of these papers indicate the need for further research.

1379. Cook, E. B. A factor analysis of acuity and phoria measurements obtained with commercial screening devices and by standard clinical methods. U. S. Navy, Submarine base, New London, Conn. Medical research laboratory. *Project NM–003–001* (*X–493*), *Rept. no. 4,* 15 August 1948, 26 pp.

1380. Duguet, J. Action de l'anoxie sur les heterophories. *Méd. aeronaut.*, 1951, *6:* 15–23.

1381. Sulzman, J. H., E. B. Cook, and N. R. Bartlett. Comparative study of measures of heterophoria. U. S. Navy, Submarine base, New London, Conn. Medical research department. *Project X–493 (Av–263–p),* 22 February 1946, 39 pp.

G. NIGHT VISION AND DARK ADAPTATION

The large number of references in this section reflects the vital significance of night visual acuity in submarine operations. Nighttime provides conditions during which the striking power of the submarine is at its maximum. It is therefore particularly important that submarine personnel possess excellent night visual capacity. Studies of night vision and dark adaptation carried out at the U. S. Submarine Base, New London, Conn., are reported in the following items: *1396, 1429, 1435, 1436, 1437, 1438, 1466, 1470, 1475, 1476, 1477, 1478, 1479,* and *1480.*

Verplanck has reported a number of tests of the radium plaque adaptometer. In field tests reported in 1943, Verplanck (*1475*) stated that the radium plaque adaptometer, as delivered, was subject to mechanical improvements, but aside from this, the adaptometer was satisfactory as a testing device. Addition of an intermediate filter was expected to improve its performance in the testing of difficult

subjects. For the proper development of necessary skill in testing personnel, supervised instruction of operators was considered essential. Modifications of the instruction manual were proposed. In 1944, Verplanck (*1476*) reported night-vision testing of 5,750 men using the radium plaque adaptometer. Of all of the men tested, 82.5 percent passed the test. Although failing a first test, approximately 60 percent passed the second test. Only 30 percent of those failing the two tests would be expected to pass a third test. Approximately 5 percent of the population failed the radium plaque adaptometer test on three consecutive tests. It was suggested by the author that these latter may constitute that section of the population who can be designated as nightblind. In 1945, Verplanck (*1477*) reported on the effect of increasing the difficulty of the radium plaque adaptometer test of night vision. It was asserted that the reliability of the test at a lower level of brightness is the same as at the standard level, and it was concluded by the author that no insignificant purpose would be served by altering the difficulty of the test. One result of increasing the difficulty of the test would be to fail a larger percentage of subjects, which would be of doubtful desirability in a test of undetermined validity.

The predictive value of the radium plaque adaptometer and other physiological measures of night vision for score on performance approximating the standing of a night lookout watch was discussed by Verplanck (*1478*) 1946. This report covered the development and use of the night lookout training stage at the Lookout School, U. S. Submarine Base, New London, Conn. On the basis of several years of experience with the night lookout trainer, it was concluded that 1 or 2 sessions on the night lookout trainer employing the basic drill serves satisfactorily to establish the fundamental habits of night lookout; namely, the use of offcenter vision. Further training sessions must stress realism and interest. These not only give additional practice in the use of night vision, but also, more important, they teach and drill correct scanning procedure. They also offer opportunity for correction of faulty reporting procedures and give greater familiarity with relative bearings. The night lookout trainer cannot be made to yield a score or other basis upon which a man's future ability as a lookout may be predicted. The trainer is not a testing device, although simulated "tests" on it may serve as a motivation of the men under training. In 1946, Verplanck (*1480*) reported on the reliability of the radium plaque adaptometer over long test-retest intervals. The radium plaque adaptometer scores of 723 men who took the radium each of two testing periods spaced more than 6 months apart were analyzed. On the basis of this work, it was possible to state that the radium plaque adaptometer test systematically separates out a small portion of the population which is unable to perform satisfactorily a test requiring adequate red vision.

The effect of night vision training on radium plaque adaptometer scores has been investigated by Orlansky (*1438*) 1945. This study was designed to ascertain if prior training on the Evelyn night-vision trainer would cut down the number of men failing the radium plaque adaptometer test. The author concluded that if there are any effects of training that can be measured by the radium plaque adaptometer they are transient in duration.

The illumination of the conning tower of the submarine is a highly important matter because of the need for preservation of dark adaptation of officers who may use the periscope. In 1946, Verplanck (*1479*) investigated the red illumination of the submarine conning tower. Verplanck's experiments were designed to provide a practical evaluation of the red illumination in the conning tower. The visual performance simulated that of an officer at the periscope and the illumination conditions invluded complete absence of lights in the conning tower, full illumination of all night lights and of all instruments in a conning tower painted black, and full illumination of all night lights and of all instruments in a conning tower painted flat white. The results of the experiments clearly indicated that without respect to the interior paint finish, the red light provided in the conning tower by two 50-watt red steamtight fixtures, although sufficient to permit casual reading and chartwork, was not sufficient to impair to any measurable extent practical night visual performance of personnel working in the conning tower.

Dark adaptation of divers has been investigated in field tests by Everly and Kennett (*1396*) 1946. Data are presented on 120 dives in water of a depth of 15 to 18 feet in which the bottom was very muddy and the tide and current conditions such as to make the advantages of dark adaptation difficult to measure. Subjective improvement was reported by 60 divers. Measurable improvement was noted in 42 dives in 170 feet of water by dark adapted divers. The practicability of dark adapting the divers by the use of dark adaptation goggles worn until the diver was on the bottom has been demonstrated.

For other reports on night vision and dark adaptation, the reference list below may be consulted.

Various factors influencing dark adaptation are discussed. Attention in the past has been given to the possibility of improving night vision by the administration of vitamin A. While it appears that deficiency of dark adaptation may be brought about by serious vitamin A lack, there is no evidence that dark adaptation of normal individuals is any way improved by addition of vitamin A to the diet, even in huge doses (*1383*).

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1392. Chapanis, A., R. O. Rouse, and S. Schachter. The effect of inter-sensory stimulation on dark adaptation and night vision. *J. Exp. Psychol.*, 1949, *39:* 425–437. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1099. [P]

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H. UNDERWATER VISION

Underwater vision is of concern to deep-sea divers and to underwater swimmers. The deep-sea diver works with an illuminating device, but even so, the visibility of objects in ocean water or river bottoms may be impaired by a number of circumstances. Jenkins, Bowen, and Rogers (*1487*) 1941 have investigated the visibility of objects in ocean water under various conditions of illumination. Attenuation by absorption and scattering and masking by the scattered light were found to be important factors. Even in the clearest water scattering is the chief factor. Because of selective absorption, color filters are of little use in increasing visibility. Tailliez, Dumas, Cousteau, Alinat, and Devilla (*1488*) 1949 have pointed out that the field of vision as seen through the porthole of the diver's helmet may be optically deformed. The factors determining effectiveness of vision in deep-sea diving are discussed by the authors.

1486. Duntley, S. Q. The visibility of submerged objects. I. Optical effects of water waves. Massachusetts Institute of Technology, Visibility laboratory. *Contract No. N5ori–07831 and NCbs–50378,* 15 December 1950, 11 pp.

1487. Jenkins, F. A., I. S. Bowen, and F. T. Rogers, Jr. Visibility in ocean water. University of California, San Diego, Calif. Radio and sound laboratory. *NDRC Rept. no. C4–sr30–024,* 18 October 1941, pp. 52.

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VIII. AUDITORY PROBLEMS

The references given in this section are principally concerned with measurement of auditory function. These references have been included chiefly as source material in connection with the section on noise and vibration (p. 129) and the section on selection of sonar operators (p. 306).

The reader's attention is particularly directed to the reports by Harris and coworkers. For studies at the U. S. Submarine Base, New London, Conn., papers by the following authors should be consulted: Harris (*1496* and *1497*) 1948 and (*1498*) 1950; Harris and Charney (*1499*) 1950; Harris and Myers (*1500*) 1948; Harris, Myers, Stover, and Stuntz (*1501*) 1949; Myers and Harris (*1508*) 1949 and (*1509*) 1950; Rose and Harris (*1516*) 1948; Stuntz (*1521*) 1950; and Wing (*1523*) 1950.

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1497. Harris, J. D. Interpretations of measurements of auditory thresholds. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 003–021, Rept. no. 1,* 12 February 1948, 7 pp.

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1504. Lifshitz, S. Fluctuation of the hearing threshold. *J. acous. Soc. Amer.,* 1939, *11:* 118–121. [M]

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1525. Anon. Recent research on hearing. *J. Amer. med. Ass.,* 1938, *110:* 900.

IX. NOISE AND VIBRATION

A. NOISE

1. GENERAL STUDIES

An examination of the literature cited in this section on noise reveals in aviation a concern for the possible pathological effects of engine noise upon hearing and sound communication. Submarine surgeons have now become aware of similar problems in submarine operations. There may be temporary loss of auditory acuity and noise may complicate intercommunication. Among the general references listed, papers by the following are recommended as particularly useful: Berrien (*1528*) 1949; Harvard University Psycho-acoustic Laboratory (*1537 and 1538*) 1950; Kryter (*1542*) 1950; Licklider (*1543*) 1949; Sabine (*1551*) 1942; Suggit (*1556*) 1947; and U. S. NRC–CAM (*1558*) 1946. The latter report lists a bibliography of 59 unpublished documents on noise, including noise measurements and control and effects of noise.

1526. Baetjer, A. M. Noise. pp. 1005–1009 in: *Rosenau preventive medicine and hygiene.* Edited by Kenneth F. Maxcy. Seventh edition. New York, Appleton-Century-Crofts, Inc., 1951, 1462 pp.

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1533. Finkle, A. L. and J. R. Poppen. Clinical effects of noise and mechanical vibrations of a turbo-jet engine on man. *J. appl. Physiol.,* 1948, *1:* 183–204. [P] [R]

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1542. Kryter, K. D. The effects of noise on man. *J. Speech Dis.,* 1950, Monogr. Suppl. no. *1:* 1–95. [R]

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1544. Lovell, G. D. Physiological and motor responses to a regularly recurring sound. *Psychol. Bull.,* 1941, *38:* 715.

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1563. Anon. Noise in industry. *Arch. ind. Hyg. occup. Med.,* 1951, *3:* 232–235.

2. PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS OF NOISE

The effects of noise upon psychological and physiological processes have been under investigation for many years. Such a study is that of Harmon (*1571*) 1933 in which mental tasks (problems in addition) were carried out in the presence of noise from specially prepared phonograph records. One was made in a busy office room with a loudness from 50 to 65 decibels, the other made on a New York City street corner with a loudness from 65 to 75 decibels. It was found that mental work, together with its physical concomitants, was accompanied by a small but consistent increase in metabolic rate, heart rate, and respiratory rate and volume. When complex noises were added, there were further increases observable at first. The increases caused by noises ran as high as 60 percent or more during the first days of the experiment. If the subject was presented with the same noise situation day after day for several weeks, the noise effects gradually disappeared and working values tended to return to normal. In the author's study there was no correlation between the attitude of the subjects and the effects of the noise.

For studies on the effects of noise on sensory functions, papers by the following should be consulted: Bogoslovskii and Kravkov (*1565*) 1941; Cassel and Dallenbach (*1566*) 1918; Rosenblith, Galambos, and Hirsh (*1577*) 1950; and Theilgaard (*1579*) 1951. The paper by Bogoslovskii and Kravkov (*1565*) is particularly interesting as an example of Russian investigations on the effect of sensory distractions on perceptual acuity.

As Archambault (*1564*) 1932 has pointed out, it can be demonstrated in many ways that noise may have damaging effects upon the functions of the nervous system. An example of such damage is to be found in the experimental sonogenic convulsions which may be produced in laboratory animals. Reports by the following may be consulted on this subject: Frings and Frings (*1569*) 1950; Frings, Frings, and Kivert (*1570*) 1950; and Mirsky, Elgart, and Aring (*1573*) 1943. Various strains of mice were subjected to sounds at a frequency of 10 kilocycles and an intensity of 110 decibels. There are interstrain and sex differences in behavior and incidence of seizure and even great individual variation in susceptibility and pattern within the same litters.

In a study of the effect of sound distraction upon memory, Morgan (*1574*) 1917 indicated that noisy conditions reduce the amount of material retained in the memory and also decrease the effective range of attention. While adaptation to noise does occur, it does not counterbalance entirely the distraction effect. The motor effects of strong auditory stimuli have been measured in man by Davis (*1568*) 1948 by recording muscular action potentials in both forearms under loud sound stimulation. In animals and man, noise has been shown to affect cardiovascular function. Ruff and Strughold (*1578*) 1939 found that exposure to noise increased the pulse rate and resulted in an elevation of systolic blood pressure. A change was also found in the patellar reflex, there being a decrease as exposure to noise continued. Yeakel, Shenkin, McCann, and Rothballer (*1583*) 1948 exposed rats for a year to the sound of a blast of compressed air for 5 minutes daily for 5 days a week. The average systolic blood pressure of gray Norway rats rose from an initial value of 113 up to 154 mm. Hg in the final 2 months of the experiment. The pressure rose from 124 to 127 mm. Hg in the controls. Sixty-four percent of the experimental rats had a mean blood pressure of 150 mm. Hg at the end of the experiments. The results suggested to the authors that the auditory stimulus increased peripheral resistance.

Laird (*1572*) 1932 has shown that in human subjects loud noises ranging in intensity from 45 to 75 decibels reduce appreciably the secretion of saliva and gastric juice necessary for the proper functioning of the digestive system. The author considers that noise is to a considerable degree responsible for the prevalence of digestive disorders in modern life. He found that sweat and aromatic foods or beverages tended to offset the depressing effects of noise on these secretions. These findings have been confirmed by Vaughan and Van Liere (*1580*) 1940 in dogs. In these experiments, dogs with Pavlov pouches were subjected to noise of 30 to 100 decibels. Frequencies of 600 cycles and 2,000 cycles were used. At 600 cycles there was a significant reduction in the volume of gastric juice secreted, but no reduction in the amount of acid. At 2,000 cycles there was a significant reduction in the amount of acid secreted. Neither frequency produced any significant change in total chlorides or in the pH of the gastric juice. The authors concluded that there are striking individual variations in the effect of noise on gastric juice secretion, and that higher pitch noises have a greater depressing effect on both volume and total acid secretion than lower pitch noises.

With the development of new types of engines and other sources of loud noises of unusual frequency, anxiety has been expressed not only for the possible damage to efficiency but also possible loss of hearing acuity and even more serious disturbances. A study of physiological effects of intense sound has been reported by Parrack, Eldredge, and Koster (*1575*) 1948. Two sound sources were used: (1) a turbojet engine (J–33–9) mounted appropriately, and (2) a special siren. The intensity of the engine sound ranged from about 120 to 150 decibels above the reference level. The siren-sound level was from about 120 to 160 decibels above the reference level. Severe, but so far temporary, losses of hearing followed exposure of project personnel to intense sound from both of these sources. During exposure the subjects reported heating of the skin, a strong sense of vibration in various parts of the body, muscular weakness, and excessive fatigue. Guinea pigs and rats were killed by exposure to intense sound of the siren for as short as 8 minutes. The apparent cause of death was excessive elevation of body temperature caused in turn by absorption of acoustic energy in the fur with conversion to heat energy. It was concluded that noise fields of sufficient intensity to impair human hearing are produced by turbojet powerplants. The frequency of the spectrum of the turbojet noise field was such that hearing loss produced in man interfered with the reception and understanding of speech. The frequencies having destructive effects on the experimental animals were within the audible range, although the effects were those usually attributed to action of "ultrasonic" frequencies. It was suggested by the authors that the important parameter may be intensity rather than frequency.

In order to explain the heating and killing of small animals in sound fields, Von Gierke, Parrack, and Eldredge (*1582*) 1950 measured the sound absorption coefficient of the rat's surface in terms of frequency. The absorption coefficient was found to decrease up to about 1,500 cycles, and then to increase up to 6,000 cycles. The behavior below 1,500 cycles was determined largely by the tissue beneath the skin, while the increase above 1,500 cycles was considered to be the result of the presence of the fur. These absorption coefficients permit the estimation of the sound energy absorbed by a whole animal. By calculating the heat balance of the animal in a sound field, the sound intensity and time required to cause temperature rise can be calculated approximately. These calculated results agree with experimental data on the heat death of rats and establish overheating as the agent responsible for death. A clothed man may be expected to absorb some sound energy in his clothing just as a rat absorbs sound energy in his fur.

For further studies on the physiological effects of noise, papers by the following should be consulted: Davis, Galambos, Hawkins, Parrack, Lurie, and Leighton (*1567*) 1942; Peyser (*1576*) 1948; and Von Gierke (*1581*) 1950.

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3. HEARING DEFECTS FROM EXPOSURE TO NOISE

For a comprehensive report on professional deafness due to exposure to noise, a paper by Larsen (*1630*) 1939 should be consulted. This comprehensive study includes a bibliography of about 200 references. In a series of 123 boilermakers whose hearing was tested with the audiometer, the maximum hearing decrement was found at 4,096 cycles. For further studies of the frequencies at which hearing is effected, several references may be consulted (*1587, 1590, 1592, 1595, 1597, 1598, 1600, 1603, 1607, 1613, 1619, 1621, 1625, 1626, 1628, 1629, 1631, 1635, 1637, 1641, 1643, 1644, 1647, 1648, 1649, 1650, 1652, 1653, 1654, 1655, 1656, 1657,* and *1661*).

Investigations of acoustic trauma in aviators indicate that the initial auditory damage tends to be manifested by a dip in the audiometer record at 4,096 cycles. The notch in the hearing curve at 4,096 cycles has been reported by many including Campbell and Hargreaves (*1590*) 1940; Castañé (*1592*) 1948; Meyer zum Gottesberge (*1637*) 1944; Ruedi and Furrer (*1649*) 1946; and von Russi (*1650*) 1946. De Wit (*1598*) 1942 carried out investigations of professional deafness among the naval air staff and submarine staff in the Swedish naval service. The submarine problem involved special features due to the noise of the diesel engines within a small space with steel resonating walls. Also, the control of equipment and apparatus in the engine-room must be made partly by spoken communication so that the ears cannot be protected. Among torpedomen and engineers in the submarine staff, it was found that professional deafness occurred in the C_5 dip (4,096 cycles). Studies of Senturia (*1655*) 1944 and (*1656*) 1949 indicate that loss of hearing among pilots may involve frequencies from 1,024 to 5,792 cycles. From studies by Bunch (*1587*) 1941, Machle (*1635*) 1947, and Senturia (*1652*) 1943, it is apparent that a frequent hearing loss for those who have been exposed to loud noises is for tones near C_4 (2,048 cycles) as well as for 4,096 cycles. Hearing loss in the region of 2,896

cycles is also stated to have a remarkably high incidence. Pastore (*1641*) 1941 found among experienced aviators that the range from 128 to 2,048 cycles was hardly affected. It was the 4,096-cycle area where pilots were most deficient. According to Dickson (*1600*) 1947 and Perlman (*1643*) 1941, the maximum dip in the audiogram is usually an octave above the frequency of the fatiguing tone. Perlman found this true for frequencies of 512, 1,024, 2,048, and 4,096 cycles. The results were not uniform for 256 cycles and a test could not be made for 8,192 cycles. A threshold curve commonly found in early acoustic trauma with a localized dip at 4,096 cycles was obtained when subjects were exposed to a fatiguing tone of 2,048 cycles. Sounds of low frequency from 64 to 256 cycles produced less acoustic trauma than those of higher frequency and of approximately equal intensity. Exposure to a fatiguing tone of 4,096 cycles did not produce a threshold curve with a localized depression at 4,096 cycles, but resulted in a curve with a localized drop for the tone an octave above it; namely, 8,192 cycles. A petrolatum-treated cotton earplug provided limited protection from acoustic trauma.

Certain kinds of noises may result in hearing defects at lower frequencies; for example, de Almeida (*1597*) 1950 reported that the apex of the deficit in hearing of subjects exposed to the noise of electric punchcard machines was recorded at a frequency of 256 cycles. In a study of the effect of intense and prolonged acoustical stimulation on the auditory sensitivity of guinea pigs, Horton (*1625*) 1934 exposed guinea pigs for 110 hours to a tone of 1,000 cycles at 125 decibels above normal human threshold. A general loss of sensitivity was found to the eight octave-tones in the frequency range from 64 to 8,192 cycles, and this loss was no more confined to one tone than to another. Tests made at intervals up to 298 days after exposure revealed no recovery from this loss. Similar findings were reported in 1935 by Horton (*1626*).

For studies on the intensity of noise required to produce hearing defects, several reports may be consulted (*1584, 1591, 1596, 1604, 1610, 1615, 1617, 1620, 1622, 1627, 1632, 1634, 1638, 1660, 1662,* and *1665*). The findings of a number of workers indicate that exposure to sound intensities of 80 to 100 or more decibels under daily working conditions for prolonged periods is likely to lead to severe auditory impairment. These conclusions are drawn from reports by Carhart (*1591*) 1950; Gt. Brit. FPRC, Otological committee (*1615*) 1950; Grove (*1617*) 1949; Jankowski (*1627*) 1950; McCoy (*1634*) 1944; Wessling (*1662*) 1948; and Wheeler (*1665*) 1951. In acute experiments on human subjects, Davis, Morgan, Hawkins, Galambos, and Smith (*1596*) 1950 exposed their subjects repeatedly at intervals of several days to intense tones of frequencies of 500, 1,000, 2,000, and 4,000 cycles at intensities of 110, 120, and 130 decibels for periods of 1 to 64 minutes. A noise somewhat resembling an airplane in flight was also employed. Temporary impairment of hearing was regularly produced, but there was no evidence of cumulative injurious effects. No significant elevation of auditory threshold was produced for tones of frequency lower than the exposure tone. The greatest hearing loss occurred at a frequency about half an octave above the exposure tone. With brief exposures the loss was sometimes confined to the two ovtaves above, but with longer exposures the hearing loss was quite extensive for all tones above the exposure frequency.

For reports relating the frequency of the hearing loss to damage of particular portions of the basilar membrane, papers by Davis, Derbyshire, Kemp, Lurie, and Upton (*1594*) 1935; Dickson and Ewing (*1601*) 1947; and Wheeler (*1664*) 1950 should be consulted. Dickson and Ewing (*1601*) point out that the basal turn of the cochlea, whose function it is to respond to high-pitched sound, is known to be highly susceptible, possibly because of its proximity to the oval window, which may expose it to the initial violence of thrusts of the stapes in response to impulsive sound. The phenomenon of high-tone deafness caused by a low-pitched engine noise may be explicable on the grounds that the chief components of engine noise are essentially impulsive and explosive in character.

Studies of Wilson (*1666*) 1943 suggest that the ears of certain persons are more susceptible to acoustic trauma than are those of others. Ears so predisposed are fatigued more readily than normal. This relationship between abnormal auditory fatigue and irreversible traumatic loss of hearing affords a means of determining in advance those persons predisposed to traumatic deafness. Such a means of screening out susceptible persons might be of great value in noisy industry or in military services. Wheeler (*1663*) 1949 has pointed out that noise exposure initiates a continuum of events ranging from reversible, temporary loss of hearing for short exposures at moderate noise levels to permanent, irreversible loss induced by exposure to excessively intense sound pressures, such as produced by blast, explosion, or concussion. A significant aim is to determine the point at which the hearing loss ceases to be reversible and becomes a permanent impairment. This determination is involved in the question of susceptibility. The noise-susceptible ear is one

which displays significantly large losses of acuity in response to noise exposure and requires a long time for recovery to normal. The author concludes that the criteria for differentiating susceptible from nonsuceptible subjects include: (1) the magnitude of the threshold shift, and (2) the recovery time from exposure. The latter is considered to have a greater differentiating value than the former.

Individual differences in sensitivity to auditory fatigue have also been studied by Peyser (*1645*) 1951 and Wilson (*1667*) 1950. Age and other factors in susceptibility to hearing loss have been considered by Fabritius (*1606*) 1948; Gruss (*1618*) 1939; Hoople, Wolfe, and Bregande (*1624*) 1948; and Lumio (*1633*) 1949.

The problem of psychogenic deafness in connection to exposure to loud sounds has been discussed by Bleguad (*1585*) 1951. In many cases the defect is purely psychogenic in origin, while in others there may be an organic lesion with a C_5 dip and a psychogenic overlay.

For further studies on hearing defects from exposure to noise, papers by the following should be consulted: Brown (*1586*) 1942; Campbell (*1588, 1589*) 1942; Causse and Chavasse (*1593*) 1943; Dickson (*1599*) 1946; Dickson, Ewing, and Littler (*1602*) 1939; Ewing and Littler (*1605*) 1935; Finch and Culler (*1608*) 1934; Firestone (*1609*) 1938; Fowler (*1611*) 1945 and (*1612*) 1947; Gt. Brit. Advisory council on scientific research and technical development, Communications committee (*1614*) 1944; Grove (*1616*) 1947; Hoople, Wolfe, and Bregande (*1623*) 1947; MacLaren and Chaney (*1636*) 1947; Miller and Taylor (*1639*) 1948; Partridge, Fletcher, and Solandt (*1640*) 1947; Pattie (*1642*) 1927; Senseney (*1651*) 1947; Rawdon-Smith (*1646*) 1935–36; Sleight and Tiffin (*1658*) 1948; Smyth (*1659*) 1932; and Theilgaard (*1660*) 1949. Reference number 1668 may also be consulted.

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4. EAR DAMAGE

Pathological changes occurring in the ear after exposure to intense noise include degeneration of the cochlear nerve (*1691*) and damage to the organ of Corti. In a report published in 1942, Davis, Galambos, Hawkins, Parrack, Lurie, and Leighton (*1567*) described the effects of exposure of guinea pigs to pure tones of various frequencies at intensities from 140 to 153 decibels. The effects of 500 and 1,000 cycles were most completely explored. The least detectable anatomical damage to the inner ear, namely, the disappearance of mesothelial cells from a limited area of the lower surface of the basilar membrane, was produced by 1,000 cycles at 140 decibels for 3 minutes. More severe and extensive damage was produced by more intense tones and longer exposures. Such damage included degenerative changes in sensory cells, rupture of the organ of Corti, and dislocation of the organ of Corti from the basilar membrane. A few days or weeks after severe exposure, the organ of Corti was found to disappear where it had been severely damaged and the nerve fibers and cells were degenerated. Milder degrees of damage were localized, but a very severe exposure (150 decibels for several minutes) caused widespread permanent damage. The damage was found to be located near the helicotrema when caused by low tones and nearer the oval and round windows for high tones. Severe and extensive damage to the inner ear was caused by loud tones without apparent injury to the eardrum or the ossicles. The authors found that cats are far more resistant than guinea pigs to inner ear injury from intense sounds. Similar findings were reported by Hawkins, Lurie, and Davis (*1680*) 1943 and Lurie, Davis, and Hawkins (*1682*) 1944. For a further report on this research, an abstract by Hawkins, Davis, and Lurie (*1679*) 1946 should be consulted.

Popoff (*1685*) 1930 subjected mice for weeks and months to a noise created by heavy hammers flattening out white-hot steel bars into scythes. The noise was graphically registered as to the prevalence of low tones (60 to 100 cycles) and high tones (2,000 to 3,000 cycles). The number of strokes of the hammer was 200 per minute. White mice were exposed for 8 hours daily for 20 days in the cage on the stand. These animals showed destructive changes at the commencement of the basilar membrane. The organ of Corti was destroyed, and changes were present in the neighboring ganglion cells. After 3 months' exposure the destructive process had extended to the higher windings of the cochlea. There was destruction of the ganglion cells with their afferent and efferent fibres within the lamina spiralis and the corresponding portion of the modiolus. After 8 or 9 months all of the ganglion cells and nerve fibers of the upper convolutions had disappeared. It was concluded that the damaging effects on the inner ear were transmitted to the auditory apparatus through bone conduction and not vibrations transmitted through the air and the external auditory meatus, since no changes were found under similar examinations in mice exposed to the same noise in cages suspended by a spring so that air transmission only was involved. Limitation of the degeneration to the superior section of the cochlea early in exposure was reported by Takezawa (*1688*) 1934 in guinea pigs exposed to noise levels of 90 to 95 decibels for 6 months. Although the degenerative changes were limited at first, after 3

months the degeneration was seen in the whole cochlea and the cochlear nerve was also involved.

That exposure of men to intense airborne sound may have deleterious effects, other than injury to the aural apparatus, is widely suspected. Exposure of animals to high-intensity sound has shown that death can be brought about if the exposure time is sufficiently long and the intensity of the sound sufficiently great. Death in this case results from the heat produced at the body surface as it absorbs the sound waves. Frings and Senkovits (*1675*) 1950 have reported inflammatory changes in the pinnae of mice subjected to high-intensity airborne sound.

Experimental studies have revealed a general correspondence between alterations in cochlear potentials and anatomical damage to the inner ear, but the parallelism is not exact or invariable. The anatomical changes are more consistent, and Davis, Galambos, Hawkins, Parrack, Lurie, and Leighton (*1567*) 1942 consider that the "electrical audiogram" (cochlear potentials) is not as satisfactory or reliable a method of assessing injury to the ear as microscopic examination. Diminution in cochlear potentials in experimental animals associated with exposure to noise has been reported by Causse and Chavasse (*1671*) 1944 and Hamburger, Hyden, and Nilsson (*1678*) 1949. The former authors exposed dogs to 1,000 cycles at an intensity of 90 and 100 decibels in an acoustic room for periods from 96 to 408 hours. The 408-hour exposures resulted in complete deafness. Other animals showed a diminution of cochlear potentials proportional to the duration of exposure. The reduction in potentials was not uniform. Diminution of sensitivity was more pronounced at frequencies of 1,300 and 4,500 cycles. In the experiments of the latter authors, cochlear potentials in guinea pigs were registered at various times after acoustic stimulation at 6,000 cycles with an intensity of 80 decibels for 3 hours. No deviations from controls were found up to 14 days after stimulation. After detonations from a revolver there were severe changes in the cochlear potentials indicating functional damage to the acoustic apparatus. Davis, Derbyshire, Kemp, Lurie, and Upton (*1673*) 1935 found that noise at a frequency of 2,500 cycles and an intensity of 95 and 105 decibels for 40 to 45 days in the guinea pig produced a fairly extensive degeneration of the outer hair cells centering in the middle of second cochlear whorl. The threshold of the electrical response was elevated corresponding to the severity and extent of the histological damage. In three cases, gross lesions of the cochlea were found to be correlated with highly abnormal electrical responses. The results indicated that the electrical respone of the cochlea is generated by the hair cells and also indicated to the authors support of the resonance theory of cochlear function.

For a discussion of the mode of origin of the C_5 dip, a paper by Ruedi and Furrer (*1687*) 1946 should be consulted. According to the authors, all natural sounds such as industrial noise have a broad-frequency spectrum, which, in the cochlear fluid, gives rise to many pairs of eddies. Each of these pairs changes direction at the perception point of approximately 4,000 cycles. At this point the basilar membrane is subjected to great tension, which can lead to permanent deformation revealed as the C_5 dip.

For further reports on ear damage, papers by the following may be consulted: Bender (*1669*) 1950; Bugard (*1670*) 1951; Causse and Falconnet (*1672*) 1947; Friedenwald (*1674*) 1913; Fujino (*1676 and 1677*) 1950; Kristensen (*1681*) 1947; Mancioli (*1683*) 1949; Nilsson (*1684*) 1950; Ruedi and Furrer (*1686*) 1946; Tissie (*1689*) 1948; Turner (*1690*) 1915; and Wolff (*1692*) 1942.

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1670. Bugard, P. Action biologique de bruits complexes de niveau élève. *C. R. Soc. Biol., Paris,* 1951, *145:* 11–12. [P]

1671. Caussé, R. and P. Chavasse. Recherches sur les potentiels cochléaires du cobaye après stimulation auditive intense. *C. R. Soc. Biol., Paris,* 1944, *138:* 847–849. [P]

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1675. Frings, H. and I. Senkovits. Destruction of the pinnae of white mice by high intensity air-borne sound. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Technical Rept. no. 6029,* September 1950, 23 pp.

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1680. Hawkins, J. E. M., H. Lurie, and H. Davis. Injury of the inner ear produced by exposure to loud tones. U. S. OSRD. Supplementary Report. 31 December 1943, 10 pp. [P]

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1683. Mancioli, G. Contributo allo studio delle otopatie professionali; richerche audiometriche sugli sbavatori. *Rass. Med. indust.,* 1949, *18:* 233–250.

1684. Nilsson, G. Det akustiska traumat ur teoretisk synpunkt. *Nord. Med., Stockholm,* 1950, *43:* 1058–1061. [D]

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5. EFFECTS OF NOISE ON EFFICIENCY

In 1948, Harris and Stover (*1699*) measured overall noise levels aboard the U. S. S. *Raton.* Interpretation of the data collected reveals that aside from the engine rooms no compartment in this submarine was noisy enough to reduce auditory acuity by a noticeable amount, or to reduce psychomotor or physiological efficiency. In the engine rooms a noise level of 108 decibels was measured at standard surface cruising speed. This was considered to be sufficient to cause auditory fatigue in some individuals and to impair communication for some hours. This loss would not be permanent. The extent of individual susceptibility was not determined. The noise spectrum in the engine room peaked at 400 cycles, which is of a type least conducive to annoyance. Even though there may be no overall quantitative effect of noise on human performance, Chapanis, Garner, and Morgan (*1696*) 1949 found evidence that subjects require more energy to perform the same kind of work in a noisy environment than in a quiet one. Several studies have shown quite consistently that the basal metabolism of subjects working in a noisy situation is higher than of those working in a quiet environment. This may account for the many reports of fatigue from workers in noisy spaces. In a report on noise in relation to efficiency, Behnke (*1693*) attributed noise fatigue to the fact of increased concentration incident to the maintenance of a satisfactory standard of work. His studies did not indicate any marked impairment resulting from noise but it was found that the subjects complained more of the annoyance or aggravation incident to work performed in the noisy room than they did of bad effects of hot atmosphere. High noise levels slowed paristaltic activity and cut down the flow of saliva and gastric juice. Disturbance of sleep was the most obvious cause of fatigue associated with noise. In an experimental investigation of the effect of change in atmospheric conditions and noise upon performance, Viteles and Smith (*1709*) 1946 stated that noise intensities up to 90 decibels were of less importance than heat. In the opinion of these authors there is no justification for expenditures to reduce noise below the 90-decibel level.

It has generally been found that noise reduces work output. Laird (*1701*) 1927 has stated that skilled workers are more adversely affected than mediocre workers. Weston and Adams (*1710*) 1932 gave a figure of 1.5 to 3 percent output loss for weavers in a noisy environment as opposed to a quiet environment. Stevens, Egan, Waterman, Miller, Knapp, and Rome (*1707*) 1941 found that most types of mental, motor, and physiological activity are affected very little by noise as such. In these experiments human subjects were subjected to continuous 7-hour periods of work in airplane noise at 115 decibels. Performance in some tasks was impaired by as much as 5 percent, but proficiency at other tests remained unaltered.

Boulin (*1694*) has commented upon the effects of noise upon industrial production. It is contended that reducing noise in workshops increases productivity and lowers defective output. Reduction in noise was also stated to lower the number of mistakes in telegraphy and typewriting. Pollock and Bartlett

(*1704*) 1932, in commenting upon the experiments in this field, stated that the results were in general agreement that noise tends to produce slight and readily recoverable diminution of efficiency. The direct effects upon nonauditory performance are commonly greatly exaggerated. Individuals react differently to noises, pleasant or distasteful. Discontinuous, loud mechanical noise was found to be more disturbing than continuous, loud mechanical noise, but even soft, pleasing, but interesting noise may be very distracting. Smith (*1705*) 1951 carried out a study on the effect of intermittent, loud noise on mental performance. The stimulus intensity was approximately 100 decibels for each subject. Bursts of sound ranged in duration between 10 seconds and 50 seconds and were administered at irregular and unpredictable intervals. It was found that the effect of bursts of intense noise upon mental performance was to increase the quantity and decrease the quality of the response. The author concluded that the allegedly malignant effects of extraneous noise may be expressed primarily in terms of depreciation in sustained performance, or of interference with factors other than adequate output. Hanley, Williamson, and Spilka (*1698*) 1950 found that the amount of noise was not systematically related to proficiency in performing mental tasks, and that such proficiency was not affected adversely or favorably by the presence of constant or variable noise. However, the tasks were simple, the noise duration short, and the levels low.

For further reports on the effects of noise on efficiency, papers by the following may be consulted: Brandt (*1695*) 1947; Gilbert and Gawain (*1697*) 1950; Hood (*1700*) 1950; Morgan (*1702*) 1917; Obata and Morita (*1703*) 1934; Stevens (*1706*) 1941; and Vernon (*1708*) 1930.

1693. Behnke, A. R., Jr. Noise in relation to hearing and efficiency. *N. Y. St. J. Med.*, 1940, *40:* 1080–1088. [R]

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1696. Chapanis, A., W. R. Garner, and C. T. Morgan. The working environment. Noise. pp. 414–417 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

1697. Gilbert, P. F. and G. C. V. Gawain. Sonic and ultrasonic effects on maze learning and retention in the albino rat. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Tech. Rept. no. 6030,* September 1950, 49 pp. [P]

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1699. Harris, J. D. and A. D. Stover. Noise levels aboard a fleet submarine. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM–003–020, Rept. no. 2,* 12 April 1948, 15 pp.

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1701. Laird, D. A. The measurement of the effects of noise on working efficiency. *J. industr. Hyg.*, 1927, *9:* 431–434.

1702. Morgan, J. J. G. The effect of sound distraction upon memory. *Amer. J. Psychol.*, 1917, *28:* 191–208.

1703. Obata, J. and S. Morita. The effects of noise upon human efficiency. *J. acoust. Soc. Amer.*, 1934, *5:* 255–261.

1704. Pollock, K. G. and F. C. Bartlett. Psychological experiments on the effects of noise. pp. 1–37 in: *Two studies in the psychological effects of noise.* Gt. Brit. MRC, Industrial health research board. *Rept. no. 65,* 1932, 70 pp. [P]

1705. Smith, K. R. Intermittent loud noise and mental performance. *Science,* 1951, *114:* 132–133.

1706. Stevens, S. S. The effects of noise and vibrations on psychomotor efficiency. U. S. NRC. Committee on sound control. *Progress report of Project 11,* 31 March 1941, 113 pp. [P]

1707. Stevens, S. S., J. P. Egan, T. H. Waterman, J. Miller, R. H. Knapp, and S. C. Rome. The effects of noise on psychomotor efficiency. Noise reduction in aircraft as related to communication, annoyance and aural injury. U. S. NRC. Committee on sound control. *Progress report of Project 2,* 1 December 1941, 126 pp. [P]

1708. Vernon, H. M. Noise. *J. industr. Hyg.*, 1930, *12:* 235. Abstr.

1709. Viteles, M. S. and K. R. Smith. An experimental investigation of the effect of change in atmospheric conditions and noise upon performance: *J. industr. Hyg.*, 1946, *28:* abstract section: 124. *Trans. Amer. Soc. Heat Vent. Engrs.*, 1946, *52:* 167–180. [P]

1710. Weston, H. C. and S. Adams. The effects of noise on the performance of weavers. pp. 38–70 in: *Two studies in the psychological effects of noise.* Gt. Brit., Industrial health research board, *Rept. no. 65,* 1932, 70 pp. [P]

6. SOUND COMMUNICATION AND NOISE

The problem of noise and speech intelligibility has been considered in a number of reports (*1732, 1735, 1736, 1738, 1739, 1743, 1744, 1745, 1746,* and *1747*). The effect on intelligibility of eliminating either the high-frequency speech sounds or the low-frequency speech sounds was determined by Pollack (*1739*) 1948 by standardized articulation-testing procedures under the special circumstances of a background of white masking noise. In general, it was found that intelligibility increased as the frequency range and the intensity level of the speech signals were increased. Speech clipping and filtering circuits in voice communication systems so distort transmitted speech as to raise the question of their effect upon intelligibilty. The results of experiments carried out by Stuntz (*1745*) 1950 indicate that speech clipping alone improves intelligibility

when the signals are partially masked by electrical noise entering the system between the transmitter and the receiver. Signals not so masked are similarly affected to almost the same degree. Intelligibility improves as clipping increases up to at least 24 decibels. Under extreme noise masking, very heavy clipping (100 decibels or more) improves intelligibility, but reduces the intelligibility of signals not so masked. Other experiments revealed that intelligibility is not likely to suffer when voice frequencies below 580 cycles are sharply attenuated, with the possible exception that when masking white noise is very intense, restoring low frequencies causes slight increases in intelligibility.

Tonndorf (*1746*) 1951 investigated the effect of three categories of noise upon the perception of sound signals: (1) conventional noises, (2) jet-powered noise, and (3) noises emanating from communication systems (static). The three kinds of noises affected the threshold of perception in different manners. Shielding by ear cushions and especially by earplugs was found to improve the ability to perceive signals in the presence of noise. As has been shown by Steer, Harris, Draegert, Hanley, and Kelly (*1743 and 1744*) 1948, speech intelligibility is generally diminished under stress. For discussions of training and other factors affecting speech intelligibility, papers by the following may be consulted: Abrams (*1711*) 1949; Chapanis, Garner, and Morgan (*1719*) 1949; Chapanis, Garner, and Morgan (*1770*) 1949; and Egan and Wiener (*1724*) 1946.

Regarding voice communication in submarines, Abrams (*1711*) suggested that operators manning the more important communication posts should be selected for their inherent ability to speak intelligibly as well as to interpret messages which have been altered by distortion and partially masked by noise. All operators can be trained to speak more intelligibly, to use their equipment efficiently, and improve their ability to interpret signals. All important messages can be standardized into short, simple, easy-to-say and easy-to-understand words. Chapanis, Garner, and Morgan (*1719, 1720*) have pointed out that one of the prime determiners of speech intelligibility is the intensity of the speech in quiet and in noise. Intelligibility of speech is determined by how much more speech energy than nose energy there is in the listener's environment. The speech-to-noise ratio is more important than the overall intensity of the noise. However, even with a constant speech-to-noise ratio, speech intelligibility can be improved if the overall system is operated at a proper gain level. Under conditions where the noise and speech are coming from the same source, this overall level can be set with a simple gain control. When the noise and speech are coming from different sources, then the overall level can be changed only by decreasing the source of the sound at or near the eardrums. Regardless of where the masking noise comes from, it has the same effect. For the same total amount of energy, speech is by far the most effective masker of other speech.

A wide variety of sounds have been investigated by Miller (*1733*) 1947 to determine the extent to which they interfere with vocal communication. The masking of speech was determined by articulation-testing methods and estimates of annoyance obtained by the method of paired comparisons. Sounds are classified as noises, tones, and voices. For all three types, the stimulus dimensions determining both masking and annoyance are the intensity, frequency or spectrum, and the temporal pattern of the sound. Masking depends primarily on the speech-to-noise ratio over the range of frequencies involved in speech. Sounds of low frequency mask this range more effectively than sounds of high frequency. Interruptions in the sound decrease the masking effectiveness. Annoyance also increases as the intensity is raised. Low-frequency sounds are less annoying than high-frequency sounds, and intermittent, irregular ones are more annoying than continuous sounds. Annoyance, however, does not interfere with vocal communications in the laboratory situation. Miller pointed out (*1734*) 1949 that the effect of an interfering noise is to raise the threshold of detectability and intelligibility and so decrease the range of intensities available for vocal communication. This shift in threshold is the measure of masking. In a study of pitch discrimination in masking, Harris (*1728*) 1948 concluded that loudness exerts a profound effect directly or indirectly on pure-tone pitch discrimination. This effect is complex and differs according to whether the tone is presented in quiet or is partially masked by noise.

For studies on the effects of noise upon loudness of speaking, papers by the following should be consulted: Black (*1713*) 1949 and (*1714*) 1951; Black and Greybiel (*1715*) 1948; Black, Greybiel, Lightfoot, and Morrill (*1716*) 1948; Broadbent (*1717*) 1951; Hanley, Draegert, Buck, and Kelly (*1727*) 1949; and Steer, Henley, Draegert, Buck, and Kelly (*1742*) 1949. Studies of Black and Greybiel (*1715*) 1948 reveal that in repeating messages heard over headsets, the listener tends to respond with greater intensity as he hears more intense signals. It is also demonstrated that vocal loudness is similarly affected when the speaker is answering questions instead of repeating words. Moreover, the subjects

were unable to maintain a constant intensity when saying back words that were heard at different levels of amplification. Two amounts of noise background introduced into the headsets of the listeners did not significantly differentiate the levels of vocal response. Messages spoken by males and females elicited different intensities of response, the female being responded to the louder. Room illumination did not affect the intensity with which the listeners repeated words. Black (*1713*) 1949 also emphasized the tendency of subjects to talk with different intensities in keeping with the level of intensity of heard stimulus. The trends were the same whether the stimuli were words to be repeated or questions to be answered. Repeated words were spoken more intensely than answers to questions heard under the same conditions. In a further study, Black (*1714*) 1951 exposed male subjects for 120 minutes to simulated cockpit noise. Following subjection to this noise there was an increase in vocal intensity which decreased linearly, but was not complete after 15 minutes of silence. Steer, Hanley, Draeger, Buck, and Kelly (*1742*) 1949 found that distracting noises fed into the headphones worn by subjects reduced the speaking rate, increased the speech time, increased the mean syllable duration, and increased the mean speech-intensity level. Similar findings were reported by Hanley, Draegert, Buck, and Kelly (*1727*) 1949. The effect of speaking and listening simultaneously has been investigated by Broadbent (*1717*) 1951. It was concluded that in general one cannot attend perfectly both to the speech of others and to our own. Whether because we are attending to what we have just said or what we are just going to say is uncertain.

Egan (*1722*) 1946 has demonstrated that although a sufficiently intense noise in one ear will mask speech heard in the contralateral ear, a weaker noise has the opposite effect, that is to say, it enhances the loudness of speech heard in the other ear. Subjects reported that the monaural speech was more dense or more crisp when noise was introduced into the contralateral ear. Most observers reported a change in the localization in the speech. It was localized nearer to the center of the head when the noise was introduced into the opposite ear. Preliminary tests indicated that the intelligibility of speech heard monaurally is slightly increased when noise is introduced into the contralateral ear. These findings have also been discussed by Egan (*1723*) 1948.

Pollack (*1740*) 1949 presented recorded speech passages against a background of white noise and against a quiet background. The effect of the noise on the loudness of speech was determined by having the listeners adjust a level of speech heard in quiet to sound equal in loudness to an assigned average level of speech presented against selected levels of background of noise. In general, it was found that low noise levels produce a proportionately lower depression in the loudness level of speech than higher noise levels. The effect of noise on the loudness of speech was found to be a function of the speech-to-noise ratio rather than of the level of the speech alone or of the noise alone. Under none of the conditons of the author's experiments did white noise actually increase the loudness of speech (the Egan effect).

For suggestions on speech reception testing, a paper by Harris (*1729*) 1948 may be consulted. Harris has also discussed (*1730*) 1950 the effect of sensation levels on intensive discrimination of noise. Loudness perception for pure tones and for speech was discussed in 1950 by Harris and Myers (*1731*). For studies of auditory discrimination in sonar operation, a paper by Neff (*1737*) 1949 should be consulted. Also a report evaluating auditory conditions in asdic cabins at sea by Solandt and Bunker (*1741*) 1944 may be referred to.

For further studies on sound communication and noise, papers by the following may be consulted: Aleksenko (*1712*) 1949, Broadbent (*1718*) 1951, Davis (*1721*) 1951, Elliott (*1725*) 1951, and Garner (*1726*) 1949.

1711. Abrams, M. H. Voice communications: personnel and phraseology. pp. 233–241 in: *A survey report on human factors in undersea warfare.* National research council, Washington, D. C., 1949, 541 pp.

1712. Aleksenko, N. I. Vliianie neakusticheskikh razdrazhenii na vospriiatie napravleniia zvuka. [Effect of nonacoustic stimulation on the perception of sound direction.] *Prob. fiziol. akust., Moskva.,* 1949, *1:* 74–88.

1713. Black, J. W. Loudness of speaking: the effect of heard stimuli on spoken responses. *J. exp. Psychol.,* 1949, *39:* 311–315. [P]

1714. Black, J. W. The effect of noise-induced temporary deafness upon vocal intensity. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine. *Project NM 001 064.01.07, Rept. no. 7,* 30 January 1951, 9 pp.

1715. Black, J. W. and A. Graybiel. Loudness of speaking: the effect of heard stimuli on spoken responses. U. S. Navy. NATB, Pensacola, Fla. School of aviation medicine. *Contract N7onr–411, Task Order no. 1, Project 20–k–2, Rept. 411–1–2 Designation Number NR–782–004,* 1 June 1948, pp. 39. [P]

1716. Black, J. W., A. Graybiel, C. Lightfoot, and S. N. Morrill. Loudness of speaking: the effect of the intensity of side-tone upon the intensity of the speaker. U. S. Navy, NATB, Pensacola, Fla. School of aviation medicine. *Contract N7onr–411, Task Order no. 1, Project 20–K–2, Rept. 411–1–4, Designation no. NR–782–004,* 12 June 1948, pp. 12. [P]

1717. Broadbent, D. E. Speaking and listening simultaneously. Gt. Brit. MRC. Cambridge. Applied psychology

research unit, the psychological laboratory. *A. P. U. 146/51,* January 1951. [P]

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1719. Chapanis, A., W. R. Garner, and C. T. Morgan. Speech. Factors influencing speech intelligibility. pp. 220–239 in: *Applied experimental psychology,* New York, John Wiley & Sons, Inc., 1949, 421 pp.

1720. Chapanis, A., W. R. Garner, and C. T. Morgan. Tonal signaling systems. Factors affecting discrimination of tones. pp. 256–261 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

1721. Davis, H. Effects of noise on human behavior and communication. *Arch. ind. Hyg. occup. Med.,* 1951, *3:* 227–231.

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7. PROTECTION AGAINST NOISE

A large volume of literature has developed on the subject of ear defenders. Walpole (*1764*) 1943 points out that the prime purpose of ear protective devices is to provide adequate insulation against high-level sound intensities so that the magnitude of the sound reaching the ear drums is reduced to noninjurious levels. Walpole described a plastic ear

defender (the acousti-guard) which consisted of a hollow disk within a plastic diaphragm. The sound enters a small hole in the outer surface of the disk, passes around the diaphragm, and out through a cylindrical hole, continuing through a fitting shaped to fit into the outer ear. A cloth pad is attached around the cylinder on the inner surface of the disk. This is provided to keep the device tight over the ear opening and thus minimize noise leakage. The device was designed to provide protection at higher sound levels by the action of the diaphragm forced against the discharge port by the pressure of the sound wave. At lower sound levels the pressure exerted is insufficient to close the diaphragm, thus permitting sound to pass through the device without serious diminution. Tests permitted the conclusion that the valve-action idea is good, but that this specific device did not have a good enough seal. Everley and Emrich (*1755*) 1944 carried out tests for estimating the sizes of ear defenders of the V–51 (R) type. These authors found that measurements of head circumference did not correlate significantly with ear-defender size. Articulation tests were conducted by Kryter (*1756*) in 1946 to determine the intelligibility of speech in the presence of noise when listeners wore earplugs (NDRC ear wardens). It was found that with a reverberating signal from a public-address system and in the presence of noise that raises the open-ear speech threshold by 60 decibels or more, the wearing of ear wardens increased the intelligibility of speech, but in direct person-to-person speech the ambient noise must be of sufficient intensity to raise the speech threshold by 80 decibels or more before ear wardens may be used without interfering with the reception of speech. Since, in some military and industrial situations, noise is generated that raises the threshold for hearing speech by more than 80 decibels, the use of suitable earplugs under these conditions will maximize the reception of speech and afford protection against the deafening, fatiguing, and annoyance effects commonly attributed to sustained, intense noise. In a study of the effectiveness of various types of ear defenders, Schneider (*1760*) 1950 found that only 2 percent of men equipped with ear defenders acquired temporary hearing loss, whereas in those ears protected only by cotton wool, the percentage of temporary hearing loss amounted to 17.3. Parrack and Eldredge (*1758*) 1951 considered that while the V–51 (R) ear defender is not perfect, it is the best all-round ear protector for most cases. Cotton wool impregnated with petrolatum and paraffin is a suitable substitute when not contaminated by grimy hands. For further studies on earplugs, papers by the following should be consulted: Allen (*1748*) 1942, Davis (*1752*) 1945, Dickson (*1753*) 1942, and Siirala (*1762*) 1949.

Borshehevskii (*1749*) 1938 has described a special helmet designed to protect against noise. This "sub-helmet," as it is called, consists of noise-resistant insulation layers, covered by soft rubber. The sub-helmet is described as easy to put on and does not interfere with the wearing of the flier's uniform and does not exert undue pressure on the helix. Wearing of the helmet is said to prevent pain in the ear and there is no stuffy feeling in the ear which is frequently observed in fliers without such protection. Several other advantages are described. In a survey of engine- and boiler-room noise on vessels of the Royal Canadian Navy, a recommendation is made by the Canadian National Research Council (*1750*) 1942 for the use of sound-absorbent material on the bulkheads. This is recommended in addition to properly fitted ear defenders.

For further reports on protection against noise, papers by the following may be consulted: Coates (*1751*) 1931, Edwards (*1754*) 1948, MacFarlan (*1757*) 1941, Perwitzschky and Lanig (*1759*) 1936, Shambaugh (*1761*) 1943, Taylor (*1763*) 1947, Watson and Knudson (*1765*) 1944, and Witheridge (*1766*) 1948. A letter describing the combat against noise which appeared in the Journal of the American Medical Association in 1929 (*1767*) may also be consulted.

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B. VIBRATION

1. PHYSIOLOGICAL EFFECTS OF VIBRATION

In an experimental study on human subjects of the physiological effects of mechanical vibration, Loeckle (*1777*) 1950 found that a rise in frequency of the vibratory stimulus was, in general, more disagreeable than an increase in amplitude. Subjective sensations were most impressive when the subject was seated and tense. The sensations are associated with uneasy, vegetative sensations, change in respiratory rhythm, tension in the lower extremities, and pain in the head. The human organism can vibrate with a critical frequency below 10 cycles per second. Above 140 cycles per second damping by the body is complete. Damping is directly proportional to the quotient of body size to body weight. Damping is better when the subject is standing. Shaking vibrations are superimposed on respiratory movements, and shaking movements of the heart and stomach may be seen on the fluoroscopic screen. Maximum subjective comfort depends not upon critical frequency or damping effect but upon alternating acceleration of the skull. Impairment of visual acuity is directly associated with the transmission factor. Lines not parallel to the direction of vibration appear vague, blurred, or broadened. Measurements of binocular vision showed that above 16 cycles per second, the phenomenon has a constant relationship to amplitude transmitted to the skull. The patellar reflex and the Achilles reflex, as well as other proprioceptive reflexes, were inhibited. In experiments to explain this reflex behavior, it was found that the reflexes were changed only quantitatively and could be revived by various facilitatory stimuli. Investigations an animals revealed no pathological changes in the spinal cord or brain. Efficiency tests on man before, during, and after vibrations showed some apathy, but little sensory effect. According to the author, injuries to health attributable to vibration have been demonstrated reliably, as yet only in men using pneumatic tools for extended periods; or workers on certain hammering machines in shoe factories. Generally speaking, men and animals are surprisingly resistant to vibration. For other general reports on the effects of vibratory motion on the human body, papers by Goldman (*1774*) 1948 and Reiher and Meister (*1781*) 1946 should be consulted.

For studies on the absorption and propagation of vibratory energy by the body, papers by the following should be consulted: Franke, von Gierke, Oestreicher, Parrack, and von Wittern (*1772*) 1951; Francke, von Gierke, Oestreicher, and von Wittern (*1780*) 1950; and Ernsthausen (*1771*) 1950. Parrack, von Gierke, Oestreicher, and von Wittern made measurements of the response of the body surface to mechanical vibrations in overlapping frequency ranges so as to span a total frequency range of 20 to 20,000 cycles per second. The results were consistent and described the mechanical impedance of the body surface and the elastic properties of the tissue. The impedance consists of a frictional resistance and reactance. The resistance was found to be proportional to the square root of the frequency. The reactance is an elastance varying inversely with the frequency up to about 50 cycles per second, where it becomes zero. Above this frequency the reactance is proportional to the frequency throughout the measured range. The vibratory energy absorbed at the body surface and converted to heat in the tissue may be calculated from the impedance. From these results the authors developed a theory on the mechanical behavior of the vibrating body tissue that considered the tissue as an elastic medium with viscosity.

For studies on the effects of vibration upon sense organs, papers by the following may be consulted: Mercier (*1778*) 1948, Temkin (*1793*) 1933, and Yamamoto (*1796* and *1797*) 1949. Experimental studies on the influence of vibration upon the auditory organ have been reported by Yamamoto *1796* and *1797*). This author applied a vibratory stimulus with a frequency of 40 cycles per second to

guinea pigs which were confined on the platc of a vibrator in free postures. The guinea pigs received 2 or 4 hours of vibration a day for a total exposure of 10 to 160 hours in different groups of animals. As the vibrator produced a noise of 150 decibels, the author subjected another group of guinea pigs to the noise of the vibrator without the vibration. Rotary nystagmus was reduced for animals receiving an exposure of 10 hours of vibration which also reduced the strength of auricular reflex. The effects were apparently due to vibration and not the noise. Histological examination of the auditory organ of the guinea pigs used in these experiments revealed atrophy of the organ of Corti, more marked in the upper than in the lower coils of the cochlea. There were few changes in the cochlear nerve and cells of the spiral ganglion. In the acoustic maculae there was reduction and disappearance of the otoliths, the otolith membrane, and the hair cells with disturbed arrangement of thc epithelium. There was disturbed arrangement and impaired clearness of the boundaries of the epithelial cells of the cristae acusticae, but little change in the nerve fibres. The effects of vibration were thus mainly on the maculae acousticae and the christae acousticae. Temkin (*1793*) 1933, in a discussion of industrial deafness, attributed severe lesions to vibrations within the environment rather than to the noise. He localized the apex of the hearing losses in the frequency of 256 cycles per second. In a discussion of the influcnce of vibration on vision, Mercier (*1778*) 1948 described reduction of visual acuity attributed to exposures of long duration (more than 1 hour) to vibration.

Investigations by Schaefer (*1783*) in the diesel-engine room of a submarine yielded vibrations of a frequency of 16 to 40 cycles per second. The amplitude of the vibration ranged between 0.05 and 0.3 mm. The largest amplitude of vibration was on the platform next to thc engines. A rubber mat reduced only the vibration amplitude. Electric-motor vibrations were not measurable. In subjects tested after duty in the engineroom, there was reduced performance on attentiveness tests, and the skin over the ankle and knee joints revealed hypesthesia. There was no change in the patellar reflexes, but a decreased accuracy in estimating weights. The studies revealed that, in the case of vibrations of 15 cycles, there is 90 percent transmission to the head. Hence aboard submarines a particularly unfavorable type of mechanical vibration occurs.

For further studies on the effect of mechanical vibration on the patellar reflex, a paper by Goldman (*1775*) 1948 should be consulted. His observations on the effect of mechanical vibration on the patellar reflex of the cat confirmed those of previous investigators that vibration produces an inhibition. Frequencies of 10 to 600 cycles per second were used and decerebrate and lumbar-sympathectomized cats were subjected to the vibratory stimuli. The inhibition of the patellar reflex was found to be independent of the autonomic nervous system and evidence was presented to support the concept that mechanical vibration acts by preempting the stretch reflex pathway. The inhibition was found to appear between 10 and 30 cycles, and to fade out between 300 and 600 cycles per second.

A number of reports have been given by Sueda on the effect of vibration upon body-weight, lifespan, and body temperature of experimental animals. In 1937, Sueda (*1787*) subjected rabbits to vertical or up-and-down vibration and other animals to a side-to-side vibration simulating lurching movement. The vibrating speed was 140 cycles per minute. It was found that the vertical vibration caused relatively slight injuries. The bodyweight decreased rather slowly at first but, after a certain period, the weight loss was arrested despite continuance of the vibrations. The body weight thus lost was not recovered, however, even after a long rest. Some animals lived for a long period under these conditions. Those subjected to the lurching side-to-side motions died after 9 to 21 days (mean, 16.5). The rate at which the body weight declined was much more rapid than in the case of the animals shaken vertically. Just before death, the weight of the animals suffered an additional sudden decrease. The same author (*1789*) in 1938 reported that administration of glucose to animals receiving continuous vibration enhanced the animals' capacity to withstand the harmful influences of vibration. If mice were subjected to alternate periods of vibration and rest of 12 hours' duration, it was found that the body weight was only slightly decreased and that repose facilitated recovery. Lurching motion in rabbits produced a gradual decrease of about 30 percent in quantity of food intake, a gradual decrease of about 50 percent in urinary output, a decrease of about 65 percent in respiratory rate, and an increase of about 10 to 20 percent in pulse rate (*1788*). Sueda (*1791*) 1939 found that rabbits subjected to lurching vibrations for 24 hours continuously exhibited a rise of body temperature of about 0.2° C. during the shaking process. The temperature quickly fell about 0.3° C. after termination of the stimulation. The effect of vibrations upon the estrous cycle of white rats has been investigated by Sueda (*1786*) 1937. Mature, femalc white rats were subjected to horizontal vibration of a frequency of 140 cycles a

minute and an amplitude of 4 cm. Animals shaken for a mean of 13.6 days suffered disturbances of the estrous cycle, but over half of them recovered rather quickly after the vibrations were stopped. Another group of animals shaken for a mean of 27.1 days exhibited a complete disruption of the cycle. After 23 days of shaking the estrous cycle of 71.4 percent of the animals was still completely interrupted while the rest were recovering poorly.

Schreiber (*1784*) 1950 subjected rats and mice to vibrations at a frequency of 160 cycles per minute and an amplitude of 4 cm. The concentration of ascorbic acid in the adrenal glands fell after shaking for one-half hour. In 2 hours, it fell to less than 30 percent of the prestimulation value. The author reported a decrease in total lipoid concentration in the adrenal cortex and stated that after one-half-hour shaking, the total white blood count was significantly increased. After 4 hours, there was a decrease in white blood count as well as the absolute lymphocyte count. The number of polymorphonuclear neutrophile cells was relatively decreased after one-half hour of shaking with a significant rise after 4 hours. After 5 minutes of shaking there was a hypoglycemia. The liver glycogen content was reduced by 50 percent 1 hour after shaking. After 4 hours there was still a reduction of liver glycogen. In chronic experiments, Schreiber (*1785*) 1950 found a reduction of weight of the pituitary, thyroid, and thymus glands. There was no change in the weight of the gonads or the adrenal glands. After shaking, there was a reduced tolerance to decompression hypoxia.

Reference may be made to a report by Restarski (*1782*) 1945 on the effect of vibration upon the dental pulp and periosteum of white rats. In the author's studies, the animals were exposed to vibration at a frequency of 2,600 cycles per minute 8 hours daily, 6 days per week for 28 days. This exposure did not affect the rate of growth of the incisor teeth or the calcification of the dentin. Histological examination of the dentin, pulp, alveolar periosteum, alveolar bone, and the structures of the temporomandibular articulation failed to disclose any greater variation of cellular changes than those occurring normally.

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1797. Yamamoto, K. Experimental studies on the influence of vibration upon the auditory organ. (II) The pathological and histological change of the auditory organ as influenced by the vibration. *J. oto-rhinolaryng. Soc., Tokyo,* 1949, *52 (7):* (Japanese text pagination), 233–237.

2. EFFECTS OF VIBRATION ON PERFORMANCE

There is some suggestion in the literature (*1798, 1799*) that vibration may result in impairment of performance and increase in fatigue.

1798. Knudsen, V. O. and I. H. Jones. The effect of audible and of subaudible vibrations on the acuity of hearing. *Arch. Otolaryngol.,* 1929, *10:* 472–479.

1799. U. S. Navy. Technical mission to Japan. Vibration effects. pp. 9–10 in: *Aero, surface, and submarine medicine and research in the Japanese Navy, Fascile M–1, Target M–06,* 4 September 1945, 72 pp.

Biology of Very High Hydrostatic Pressures

In the first volume of this Sourcebook (pp. 85–89) there is to be found a discussion of the literature on the effects of raised hydrostatic pressures upon the activity of living cells and tissues as well as upon biochemical reactions. It is not intended in the present volume to cover this literature again since the subject lies at the fringe of interest in compressed air, diving, and submarine medicine. Attention may be called, however, to three representative reports.

Boyd (*1800*) 1946 has investigated the effect of high hydrostatic pressures on hemagglutinating antibodies. It was found that pressures of the order of magnitude which have previously been found to coagulate proteins will destroy anti-A agglutinins investigated. Destruction was found to be complete at pressures above 4,000 atmospheres. A definitely higher pressure was required to destroy anti-Rh "blocking" antibody than was required for anti-Rh agglutinating antibody or anti-A or anti-B agglutinins. The author's results seemed to indicate that the effect of high pressures on plasma proteins is not to break up the molecules but to induce polymerization. Johnson and Schlegel (*1802*) 1948 found that high hydrostatic pressures up to 10,000 lbs. per sq. in. have no appreciable effect on the hemoglobin-oxyhemoglobin equilibrium of 0.1 percent bovine hemoglobin in 0.8 percent sodium chloride solution.

The effect of high pressures on the activation of chymotrypsinogen by trypsin has been studied by Curl and Jansen (*1801*) 1950 in connection with a general investigation of the effect of high pressures on enzymes; in particular, crystalline proteinases. Chymotrypsinogen was not activated by pressure in the absence of trypsin. No significant change in the extent of activation by trypsin was found under pressures up to 700 bars. About 10 percent less activation than in an unpressed system was observed under a pressure of 1,000 bars. The inhibition of the reaction increased with increase in pressure and practically no reaction occurred at 3,000 bars. Up to this pressure the activation proceeded after release of the pressure at practically the same rate as initially in the control. Following release of systems at higher pressures than this, progressively less activity was obtained, until after pressing at 5,700 bars on active enzymes was formed. The effect on the mixture of chymotrypsinogen and trypsin was much greater than on either protein alone.

1800. Boyd, W. C. The effect of high pressures on hemagglutinating antibodies. *J. exp. Med.*, 1946, *83:* 401–407.

1801. Curl, A. L. and E. F. Jansen. Effect of high pressures on activity of proteinases. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 165.

1802. Johnson, F. H. and F. M. Schlegel. Hemoglobin oxygenation in relation to hydrostatic pressure. *J. cell. comp. Physiol.*, 1948, *31:* 421–425. [P]

Diseases and Accidents in Submarine Personnel, Divers, and Compressed Air Workers

I. DISEASES AND ACCIDENTS IN NAVAL PERSONNEL: MORBIDITY

Pugh (*1809*) 1950 has drawn attention to the fact that colds, constipation, and skin diseases constitute the principal disorders suffered by submarine personnel. At the time of departure on a patrol, a few members of the crew may have upper respiratory infections. Infection is spread to others within 48 hours, but by the end of a week or perhaps longer, the incidence of upper respiratory infections subsides. Colds remain infrequent for the remainder of the patrol and the incidence does not rise again normally until new contacts are made. Constipation is probably the result of lack of physical exercise, a diet of starchy foods, and natural reluctance to use the cold, clammy, cramped, wet watercloset. Heat rash and fungus growth present a problem in hot, humid atmospheres and bunk sharing helps spread these conditions. Venereal disease necessitates removal of personnel in peacetime. During wartime, when removal is not carried out, there is created a detriment to morale which taxes the ingenuity of the pharmacist's mate. Vertical ladders, narrow passageways, and slippery decks are productive of falls, and operation of machinery may add to the incidence of injuries from other causes. Pugh refers also to hazards to personnel arising from the use of the snorkel. In some cases the change in atmospheric pressure produced by closing of the valve may cause ear pain and even some otological damage. In normal snorkeling operations, however, experience has revealed that little or no discomfort is experienced. Hazards associated with escape from a disabled submarine are discussed. Escape may be attempted either by the submarine escape apparatus (the "lung") or without apparatus (free escape). In the latter mode of escape, the escapee exhales during the entire ascent through the water. Failure to breathe out during the ascent may be followed by rupture of the alveoli, leading to air embolism with grave consequences. Pugh points out that World War II submarine experience indicated that it was unprofitable to keep submarines on patrol longer than 60 days. There seems to be a definite correlation between efficient endurance and the amount of time spent submerged. Either the fact of decreased endurance must be accepted or personnel selection methods must produce persons of exceptionally high endurance. The importance of sound selection techniques is stressed.

Insight into the medical problems of submarine patrols is given by reports of the following authors: Duff (*1803*) 1947, (*1804*) 1949, Duff and Shilling (*1805*) 1949, and Shilling and Duff (*1812 and 1813*) 1947. Duff (*1803*) has pointed out that only 62 deaths occurred in submarine operations in World War II, exclusive of deaths in the case of 52 overdue submarines. Twenty-six persons were lost by asphyxiation, 17 were drowned over side, 12 were killed in battle, 3 were killed by accidents, 1 committed suicide, 1 died of malignancy, 1 of pneumonia, and 1 died of unknown causes. Twenty-nine patrols returned because of illness. A large number of patrols returned because of excessive personnel fatigue, carbon monoxide poisoning, and battle casualties. Four patrols returned because of a limitation of potable water supply. Of injuries encountered in submarine patrols, poorly illuminated hatches accounting for many. The temperature in the submarine sometimes rose to 125° F. in the maneuvering room during "silent" running. With a sea temperature of 27° F. the single hull portions of the boat could not be heated adequately. Ice formed in the bilges and in pipes containing water, such as the shower drains. Cold, rough weather, and seasickness reduced morale in some

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patrols as did lack of targets. Duff (*1804*) states that excessive fatigue limited the duration of 9 patrols. Illness due to carbon monoxide poisoning limited the duration of 6 patrols. In 5 patrols, battle casualties caused the patrol to be curtailed, while in 2 patrols a case of acute appendicitis was the limiting factor. The following conditions limited the duration of 1 patrol each: multiple axphyxiation, serious injury, pneumonia, mumps, mental disease, copper sulfate poisoning, and unknown fever. Duff and Shilling (*1805*) reported disturbances of the digestive tract and urogenital system. The incidence of tuberculosis was low, being 0.43 percent. Shilling and Duff (*1812*) points out that the pharmacist's mate is medical officer, dentist, nurse, and chaplain all rolled in one. In 685 patrols studied by Shilling and Duff, some 1,208 injuries were considered sufficiently important to justify mention in the official patrol report. Injuries were listed in the following decreasing order of frequency: lacerations, contusions, sprains, abrasions, burns, shrapnel and gunshot wounds, fractures, and heat exhaustion. Many crew members sustained injury on the bridge watch where extremely rapid maneuvers were necessary to clear the bridge in seconds or where heavy seas flung the men against the steel surfaces. The routine of checking the torpedoes was also hazardous and resulted in 1 fatal intracranial injury. One hundred and ten submarines in 200 pickup operations recovered 542 aviators. Ten percent of these airmen were suffering from severe wounds and shock, but only 2 of the aviators died on board.

Gastric and gastrointestinal disturbances and constipation are common in submarines, and occasional cases of acute appendicitis occur. These are a cause of anxiety to submariners. Diagnosis is difficult to make sometimes because of frequent gastrointestinal disturbances in submariners. Conservative treatment is recommended. With conservative treatment more cases will recover than if surgery is atttempted aboard the submarine. No food is to be given by mouth; fluid may be given by mouth or intravenously. Cathartics must never be administered. The patient is to have absolute bed rest, sedation to produce quiet sleep, and an icebag over the lower right quadrant of the abdomen. Antibiotics should be given in adequate doses. During World War II pharmacist's mates made the diagnosis of acute appendicitis in 127 instances on 116 war patrols. There were no fatalities. In 11 cases the patrols were terminated and it was stated in 10 of these that the appendix would have ruptured if the submarine had not returned. The performance of three appendectomies aboard submarines has been reported. As previously stated, this procedure is contraindicated since it carries with it a higher mortality than conservative treatment under submarine operating conditions.

The influence of weather, combat, and overcrowding on the rate of incapacitation from disease and accident aboard 9 ships of the line has been studied and reported by Morales and Tarver (*1808*) 1946. Most of the major types of vessels are represented in the study. With regard to respiratory diseases, cold weather increased the incidence, whereas neither overcrowding nor combat seemed to produce any observable effect on incidence. The incidence of gastrointestinal diseases was not affected by overcrowding or combat, but was somewhat more prevalent during steady hot weather. Skin diseases seemed to be more prevalent in hot weather, but were unaffected by overcrowding or combat. The number of accidents was slightly higher during the months of steady hot weather, and was slightly higher during combat but was not affected by overcrowding.

Schaefer (*1810*) 1948 has reported on health conditions in German submarines. It was stated that during the first few weeks of a cruise 68 percent of the men lost weight, even though on restricted activity. The men of the deck force showed the earliest loss of weight and later the engineering force. Three weeks were required for the diesel- and motor-room force to regain their weight. Members of the crew began to lose weight later than the officers, and this was attributed to the greater psychic strain under which the latter were believed to be operating. Tonndorf (*1814*) 1948 reports that, in the first phase of World War II, radio operators performed medical services aboard German submarines. This was arranged so that they would be familiar with symptoms and terms when radioing for instructions for the care of the sick. The medical manual for submarines was considered insufficient because of lack of detailed instructions. Laymen performed such procedures as setting a broken bone, opening an abscessed gum, and amputating a foot. All were described as successful. Anesthesia was by morphine and oral administration of alcohol. In 1942, a naval surgeon was attached to every submarine tender, 1 for every 10 submarines. Later on, medical assistants were trained to take over duties of the medical officers aboard submarines. These assistants began to man the submarines in 1944. They were trained in naval hospitals and had 2 months special training on submarine problems. Information on health conditions on Japanese submarines is given by Tonndorf (*1814*) and also in a U. S. Navy, ONI report (*1816*). It appears that

there was a high incidence of pulmonary tuberculosis among Japanese submariners.

For further studies on special medical problems aboard submarines, papers by the following may be consulted: Ingraham and Wheeler (*1806*) 1943, Shilling and Kohl (*1811*) 1947, and U. S. Navy, BuNavPers (*1815*) 1949.

1803. Duff, I. F. Medical aspects of submarine warfare in the human factor as reflected in war patrol reports. pp. 156–183 in: *History of submarine medicine in World War II.* Edited by Shilling, C. W., and J. W. Kohl. U. S. Navy. Submarine Base, New London, Conn. Medical research laboratory. 25 May 1947, 328 pp.

1804. Duff, I. F. Medical aspects of submarine warfare. *Arch. intern. Med.,* 1949, *84:* 246–260. [R]

1805. Duff, I. F. and C. W. Shilling. Medical care on wartime operating submarines. *Nav. med. Bull., Wash.,* 1949, *49:* 580–591.

1806. Ingraham, H. S. and S. M. Wheeler. Study of respiratory infections on submarines with special reference to the spread of infection through the air. U. S. Navy. NMRI. *Project X–45* (*Sub. no. 15*), 25 February 1943, 38 pp.

1807. Knap, J. *Laerebok i skipshygiene og skipsmedisin.* Oslo, Johan Grundt Tanum, 1948, 327 pp.

1808. Morales, M. and E. Tarver. The influence of weather, combat status, and overcrowding on the incidence of disease and accidents aboard naval vessels. U. S. Navy. NMRI. *Research Project X–205, Report no. 5,* 9 April 1946, 18 pp. [R]

1809. Pugh, L. Medical problems encountered in undersea craft. *J. Amer. med. Ass.,* 1950, *144:* 230–233. [R]

1810. Schaefer, K. E. Technical influences. IV–D. The process of adaptation to the entire environment of submarines. pp. B: I–59—B: I–79 in: *Monograph on submarine medicine, Folio I.* Germany, U. S. Zone. Office of naval advisor. 1948.

1811. Shilling, C. W. and J. W. Kohl. Special care of submarine personnel. pp. 63–76 in: *History of submarine medicine in World War II.* U. S. Navy. Submarine Base, New London, Conn. Medical research laboratory, 25 May 1947, 328 pp.

1812. Shilling, C. W. and I. F. Duff. Analysis of patrol reports: surgical care on a wartime operating submarine. pp. 94–114 in: *History of submarine medicine in World War II.* Edited by Shilling, C. W., and J. W. Kohl. U. S. Navy. Submarine Base, New London, Conn. Medical research laboratory. 25 May 1947, 328 pp.

1813. Shilling, C. W. and I. F. Duff. Medical care on wartime operating submarines. pp. 115–156 in: *History of submarine medicine in World War II.* Edited by Shilling, C. W., and J. W. Kohl. U. S. Navy. Submarine Base, New London, Conn. Medical research laboratory. 25 May 1947, 328 pp.

1814. Tonndorf, J. The medical service on the submarines. Germany, U. S. Zone. Office of naval advisor. pp. A: 1–9 in: *Monograph on submarine medicine, Folio I,* 1948. *History of medical service of German armed forces.* Edited by W. Kittel. U. S. Naval forces. Germany. Technical section (medical), 12 May 1948, 105 pp.

1815. U. S. Navy. BuNavPers. (B) Medical problems in submarines. pp. 142–150 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp.

1816. U. S. Navy, ONI. Germany, U-boat medical research. *O. N. I. serial no. X–1250,* 21 June 1945, 1 p.

II. EAR, NOSE AND THROAT DISTURBANCES

A. GENERAL STUDIES OF OTORHINOLARYNGOLOGICAL DISTURBANCES

Sternstein (*1826*) 1946 has presented a description of the common ear, nose, and throat conditions of clinical importance to the naval medical officer, not trained in the specialty, who may be assigned to independent duty. The paper discusses practical measures necessary for effective management of otorhinolaryngological disturbances. Consideration is given to otitis media among aviators, submariners, and divers.

A paper by Tonndorf (*1827*) 1948 on the influence of service on submarines on the auditory organ may be consulted. This paper discusses the effects of pressure variations within the submarine, particularly on snorkel operations in which transient ear disturbances may occur. In some cases there is vascular injection of the tympanum after being at sea for many days. The phenomena are transient and cannot be demonstrated by audiometer tests after return to the base. In the author's experience, the irritation of the tympanum disappeared after 3 to 4 weeks at sea. Cases of acute otitis media are described, including suppurative cases. German submarine trainees underwent tests in the diving tank. Only 1 percent of men undergoing diving training suffered ear disorders. Four percent of the personnel complaining of the ear trouble during diving training had acute purulent otitis media. The author describes eczematous conditions of the external ear, furuncles, and other conditions. For other papers giving an introduction to the general subject of ear, nose, and throat disturbances, papers in the reference list given below should be consulted.

1817. Eagle, W. W. Secretory otitis media. *Ann. Otol., etc., St. Louis,* 1946, *55:* 55–67. *Trans. Amer. Laryng. rhin. otol. Soc.,* 1946, 23–37. [CH]

1818. Farrior, J. B. Lymphoid eustachian salpingitis: its effect on tubal patency. *Arch. Otolaryng., Chicago,* 1948, *48:* 221–232. [CH]

1819. Hayashi, S. Statistic study of mastoid cell development in cases of chronic otitis media, as observed in X-ray pictures. *J. oto-rhinolaryng. Soc., Tokyo,* 1951, *54* (*6*)*:* (English text pagination), 28–29.

1820. Hitschler, W. J. The relationship of swimming and diving to sinusitis and hearing loss. *Laryngoscope, St. Louis,* 1949, *59:* 799–819.

1821. Hoople, G. D. Otitis media with effusion—a challenge to otolaryngology. *Laryngoscope, St. Louis,* 1950, *60:* 315–329.

1822. Kurozumi, S. What influences on the hearing acuity were found when the pressure in the tympanic

cavity was changed experimentally? *Nippon zibiinkoka gakkai kaiho,* 1950, *53:* (Japanese text pagination), 331–335; (English text pagination), 35–36. (In Japanese with English summary.) [P]

1823. Lewis, R. S. Common accidents to the ears and their treatment. *Med. Pr.,* 1948, *219:* 579–582.

1824. Ortiz, R. B. Barotrauma otico. *Rev. Otorrinolaring.,* 1948, *8:* 41–66. (English summary.)

1825. Simpson, W. L. and J. E. Witcher. A study of the eustachian tubes and their orifices and lumens in patients with large operative defects giving direct visualization. *Ann. Otol., etc., St. Louis,* 1947, *56:* 357–367.

1826. Sternstein, H. J. Management of common eye, ear, nose, and throat conditions in naval practice. *Nav. med. Bull., Wash.,* 1946, *46:* 1041–1052.

1827. Tonndorf, J. The influence of service on submarines on the auditory organ. pp. D II–1—D II–54 in: *Monograph on submarine medicine.* Germany, U. S. Zone. Office of naval advisor. 1948. [R] [CH]

B. OTOLOGICAL EFFECTS OF COMPRESSION AND DECOMPRESSION

Two papers on the effects of pressure variations in snorkel operations upon the clearing of the middle ear are cited. The first study, by Irvine (*1833*) 1950, reports observations made during an Arctic snorkel cruise of H. M. submarine *Ambush* in 1948. During pressure changes, 17 out of 19 sleeping men were awakened. Seven of these had difficulty in clearing the ears and eight of the men showed injection of the tympanic membrane. One man had a bilateral serous effusion. In an experimental study on an anesthetized goat, it was found that under pressure the animal behaved in a manner similar to human beings. The animal was taken to an equivalent depth of about 30 feet of water. No change was noted in the mouth of the Eustachian tube under direct visualization at the onset of the pressure drop, but later the mouth of the Eustachian tube opened and the tube cleared, a stream of bubbles being seen to issue forth from the mouth of the tube. Once the tube had cleared, the mouth shut down and remained closed until the next clearing. The clearing of the tube occurred at a pressure difference about 1 to 1¼ lbs. per sq. in. This was repeated at similar intervals until atmospheric pressure was again reached. No swallowing movements occurred while the pressure was decreasing.

Uffenorde (*1840*) 1948 reported that otological examinations of men returning from snorkel operations in German submarines revealed turbid tympanic membranes which were highly retracted and not transparent. There was an increased vascular injection of the ear membranes, and sometimes circumscribed hemorrhages were observed. Only one-fourth of all the eardrums inspected were normal. In one-third of the men, hearing impairments were proven by whispered voice and tuning-fork tests.

Behnke (*1828*) 1945 has pointed out that, in decompression, release of air from patent sinus and middle-ear cavities can take place almost instantaneously without abnormal symptoms. Equalization of pressure between the middle ear and the external atmosphere is more difficult during compression. The nature of the valvular action of the Eustachian tube in relation to changes of atmospheric pressure has been investigated by McGibbon (*1837*) 1947. In these studies, passive opening of the Eustachian tube recurred on an average at each successive decrement of extratympanic pressure corresponding to an ascent of 435 feet. Closure took place immediately, leaving a residual intratympanic positive pressure of about 3.6 mm. Hg. Less than 3.6 mm. Hg pressure is insufficient to maintain passive patency of the tube. Schubert (*1839*) 1950, in a study of the resistance of the eardrum to high pressure, carried out experiments on cadavers in which 23 normal tympanic membranes ruptured at a maximum pressure of 1,292 mm. Hg and at a minimum of 532 mm. Hg. In tympanic membranes presenting atrophic scars, the highest pressure for rupture was 380 mm. Hg, the lowest being 304 mm. Hg. The maximum pressure to be safely endured by a normal tympanic membrane amounts to about 160 mm. Hg, according to the author.

Three reports on pressure changes and barotrauma in the middle ear of monkeys resulting from decompression and recompression have been given by Chang, Margaria, and Gelfan (*1830, 1831*) 1949 and (*1832*) 1950. Pressure changes in the middle ear of 12 monkeys during decompression and recompression were measured directly by means of a membrane-mirror manometer and recorded. During a slow rate of decompression (50 mm. Hg per minute), the Eustachian tube opened periodically to keep the tympanic pressure always close to the ambient pressure. A differential pressure of about 52 mm. Hg was required to open the Eustachian tube initially. Thereafter, the required pressure was less, apparently diminishing gradually toward the later stages of decompression. A decompression rate greater than 120 mm. Hg per minute resulted in a sustained patency of the Eustachian tube. At the instant of explosive decompression, the middle-ear pressure increased abruptly to a value which tended to approach the pressure difference between the pre- and post-explosive decompression altitudes and then to return quickly to ambient pressure. During recompression, anesthetized monkeys were not able to equalize the tympanic and ambient pressures, and there developed in the middle ear a negative pressure, the magnitude of which was determined by the range of recompression.

Unanesthetized monkeys were able to accomplish pressure equalization by active opening of the Eustachian tube unless they were subjected to very fast recompression rates. The critical negative pressure for tympanic hemorrhage was about 300 mm. Hg. A negative pressure of 38 mm. Hg over a prolonged time led to the same degree of damage as the higher negative pressure.

For studies on the effects of barometric pressure changes on hearing, papers by the following may be consulted: Jones and Edmonds (*1834*) 1949; Kos (*1835*) 1945; Rasmussen (*1838*) 1946; Wever, Lawrence, and Smith (*1841*) 1948 and (*1842*) 1949. For other studies on the effects of changing barometric pressure, the following references should be consulted: 1829, 1836, and 1843.

1828. Behnke, A. R. Physiologic effect of pressure changes with reference to otolaryngology. *Arch. Otolaryng., Chicago,* 1945, *42:* 110–116.

1829. Byrne, J. G. *Studies on the physiology of the middle ear.* H. K. Lewis & Co. Ltd., London. 1938, 298 pp.

1830. Chang, H. T., R. Margaria, and S. Gelfan. Pressure changes and hemorrhage in the middle ear of monkeys resulting from decompression and recompression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1949, *8:* 23. [P]

1831. Chang, H. T., R. Margaria, and S. Gelfan. A quantitative study of pressure changes in the middle ear of monkeys and otitic barotrauma resulting from decompression and recompression. Yale aero-medical research unit, Yale University School of Medicine. *Navy contract N6–ORI–44, Task Order VIII,* 16 April 1949, 33 pp. [P]

1832. Chang, H. T., R. Margaria, and S. Gelfan. Pressure changes and barotrauma resulting from decompression and recompression in the middle ear of monkeys. *Arch. Otolaryng., Chicago,* 1950, *51:* 378–399. [P]

1833. Irvine, G. S. Report of an investigation into the clearing of the eustachian tube in unconscious (anaesthetised) goats. Gt. Brit. MRC–RNPRC, UPS. *R. N. P. 50/5ol, U. P. S. 112,* February 1950, 5 pp. [P]

1834. Jones, M. F. and F. C. Edmonds. Acoustic and vestibular barometery. Air pressure effects on hearing and equilibrium of unoperated and fenestrated ears. *Ann. Otol., etc., St. Louis,* 1949, *58:* 323–344. [P]

1835. Kos, C. M. Effect of barometric pressure changes on hearing. *Arch. Otolaryng., Chicago,* 1945, *41:* 322–326. [R]

1836. Lieberman, A. T. Aero-otitis media in pressure chamber "flights." *Arch. Otolaryng., Chicago,* 1946, *43:* 500–507.

1837. McGibbon, J. E. G. The nature of the valvular action (passive opening) of the eustachian tube in relation to changes of atmospheric pressure and to aviation pressure deafness. pp. 53–59 in: *Contributions to aviation otolaryngology* by E. D. D. Dickson. London, Headley Brothers, 1947, 257 pp. [R]

1838. Rasmussen, H. Studies on the effect upon the hearing through air conduction brought about by variations of the pressure in the auditory meatus. *Acta otolaryng., Stockh.,* 1946, *34:* 415–424. [P]

1839. Schubert, H. Über die Widerstandsfähigkeit des Trommelfells gegen Überdruck der Aussenluft. *Z. Hals-Nas.-u. Ohrenheilk.,* 1949, *1:* 357–358. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 945.

1840. Uffenorde, H. Otological experience with "Schnorchel" equipped submarine. D III–1—D III–41 in: *Monograph on submarine medicine Folio VII.* Germany, U. S. Zone. Office of naval advisor. 1948 [P] [CH] [R]

1841. Wever, E. G., M. Lawrence, and K. R. Smith. The middle ear in sound conduction. *Arch. Otolaryng., Chicago,* 1948, *48:* 19–35. [P]

1842. Wever, E. G., M. Lawrence, and K. R. Smith. The effects of negative air pressure in the middle ear. *Ann. Otol., etc., St. Louis,* 1949, *57:* 418–428. [P]

1843. Anon. Effect of changing barometric pressure. Flight Surgeon's Reference File. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *AAF Manual 25–0–1, 8–3–1/8–3–6,* 1 November 1945.

C. AEROTITIS MEDIA AND AEROSINUSITIS

Barometric pressure changes occurring in diving and also in snorkel operations may be of sufficient magnitude to cause inflammation of the middle ear and sinuses. These effects on the middle ear and sinuses may range from minor hyperemia to serious pathological changes with effusion, hemorrhage, suppuration, and rupture of the eardrum. There is an extensive amount of literature on aerotitis media and aerosinusitis, and a rather wide selection from this literature has been included in the reference list given below. In the U. S. submarine service, investigations of aerotitis media have been principally carried out in connection with the selection and indoctrination program at the escape training tank, U. S. Submarine Base, New London, Conn., and the diving schools.

In 1944, Shilling (*1876*) presented a report on aerotitis media and auditory acuity loss in submarine escape training. This paper presents an analysis of the extent of the damage associated with submarine escape training and outlines possible preventive and therapeutic procedures. Thirty percent of the men undergoing escape training at New London were found to have difficulty leading to aerotitis media and resultant loss of auditory acuity. Of the 152 cases diagnosed as aerotitis media in the series under consideration, 18 of the more severe cases showed an average drop in acuity of 12.7 to 23.9 decibels as compared with a control group. By otoscopy and nasopharyngoscopy, it was possible to predict with fair accuracy which ear would suffer damage during the 50 lbs. pressure test. By means of a thorough preselection examination combined with a routine check on the ability of each subject to perform the Valsalva maneuver, a group could be selected in which otopathology could be reduced to 2 to 3 percent of the cases instead of the 27.5 to 30 percent found in 2 separate groups of 858 and 708 men. It was found that for low

tones the ears were relatively unaffected, but, for tones of 2,046 and above, a loss of acuity was the rule for ears affected by pressure. In some cases permanent damage may result. However, in some ears with considerable otopathology, the losses in acuity may be slight. In all the cases with severe damage to the ears, the author noted flattening of the Eustachian-tube orifices caused by lymphoid hyperplasia. It was thus predicted that X-ray or radium treatment of the Eustachian orifice should be of benefit. It was stated that, with more careful preselection of candidates and proper administration of pressure, severe otopathology with associated hearing loss need not be as common as formerly. Shilling, Haines, Harris, and Kelly (*1877*) 1947 stated that the effect on auditory acuity was actually less than might have been anticipated and very severe loss in hearing acuity was associated only with maximum damage to the drum and with effusion into the middle ear.

A report by Haines and Harris (*1861*) 1947 is based on a study of 6,149 submariners examined by means of the otoscope, the nasopharyngoscope, and the audiometer before and after they were given the 50 lbs. pressure test at the escape training tank. Five experimental groups were given different types of treatment: (1) psychological treatment, (2) topical treatment, (3) X-ray treatment, (4) radium treatment, and (5) treatment of dental malocclusion. Only slightly beneficial effects resulted from tropical treatment consisting of 5 drops of 0.25 percent neosynephrine in an isotonic solution applied to the nasopharynx every 2 hours or several hours before the pressure test. The results of X-ray therapy to the Eustachian tube were inconclusive. The radiumtherapy consisted in the application for 8 to 10 minutes to the nasopharyngeal orifice of the Eustachian tube a small metal cylinder containing 50 mg. of radium salt. This dose after two to eight applications at intervals of a month was found effective in reducing the amount of lymphoid tissue around the opening of the Eustachian tube. Ninety percent of the patients thus treated became able to sustain pressure without developing aerotitis media. Dental therapy was investigated in cases in which improper jaw motion was suspected of hindering normal opening and closing of the Eustachian tube. Striking success was reported for this procedure.

For another report on aerotitis media based on experience at the U. S. Submarine Base, New London, Conn., a paper by Teed (*1879*) 1949 may be consulted. A case history is given in detail and the author describes four grades of severity of the condition. He prefers the term "salpingotympanitis" rather than "aerotitis media" in that the former term emphasizes the important role of the Eustachian tube in the evolution of the disease. In grade I, blood vessels expand, congestion is noted, and the eardrum is retracted. If the subject is removed from pressure at this stage, congestion and pain disappear. A vasoconstrictor drug helps to relieve pain. In grade II, the eardrum is retracted and red in all quadrants, and the patient complains of severe otalgia and loss of hearing. Catheterization of the Eustachian tube may correct retraction of the drum, but will not reduce inflammation or pain. It is evident that the blood vessels in this grade have expanded beyond the limit of nervous control and are temporarily paralyzed. Time only will bring about return of adequate vascular function. The author recommends sedation and bed rest. In grade III, there is transudation of serum and the tympanum may be completely filled with fluid causing the eardrum to have a yellow appearance. Decrease in expansion of the blood vessels in this grade may be due to a splinting action of the fluid or to tissue edema. Treatment consists of daily shrinkage of the tubal mucosa and inflation of the Eustachian tubes. If fluid is not absorbed within a week, myringotomy, followed by suction, is indicated. About 0.5 percent of men passing through the training tank at New London developed so-called grade IV salpingotympanitis characterized by hemorrhage into the middle ear and/or perforation of the eardrum. The entire middle ear may be filled with blood and the eardrum appear black. Dissecting hemorrhages may occur in the eardrum with rupture into the external canal.

1844. Aschan, G. K. Aero-otitis media and aerosinusitis. *Acta otolaryng., Stockh.*, Suppl., 1946, *69:* 1–116. [P]

1845. Ballenger, W. L., H. C. Ballenger, and J. J. Ballenger. Injuries and diseases of the tympanic membrane. pp. 637–641 in: *Diseases of the nose, throat and ear.* Philadelphia, Lea & Febiger, 1947, 993 pp.

1846. Ballenger, W. L., H. C. Ballenger, and J. J. Ballenger. Diseases of the Eustachian tubes. pp. 642–651 in: *Diseases of the nose, throat and ear.* Philadelphia, Lea & Febiger, 1947, 993 pp.

1847. Bateman, G. H. The effect of sinusitis on flying personnel. pp. 162–172 in: *Contributions to aviation otolaryngology.* By E. D. D. Dickson. London, Headley Brothers, 1947, 257 pp.

1848. Bierman, H. R. and I. W. Brickman. The relationship of dental malocclusion to vacuum-otitis media and the use of dental splints during descent from altitudes. *Ann. Otol., etc., St. Louis*, 1946, *55:* 5–12. [P]

1849. Boies, L. R. Acute otitis media. pp. 61–69 in: *Fundamentals of Otolaryngology.* Philadelphia, W. B. Saunders Company, 1949, 443 pp.

1850. Caneghem, ( ) van. La pathogénèse des déviations successives de la tête au cours des otites aigües. *Acta oto-rhino-iaryng., Belg.*, 1947, *1:* 270–274. [D]

1851. Carruthers, D. G. Diseases of the middle ear. pp. 201–210 in: *Diseases of the ear, nose, and throat.* Baltimore, The Williams & Wilkins Co., 1948, 344 pp.

1852. Carruthers, D. G. The complications of suppurative otitis media. pp. 211–288 in: *Diseases of the ear, nose, and throat.* Baltimore, The Williams & Wilkins Co., 1948, 344 pp.

1853. Chester, L. and J. C. Drooker. Aero-otitis media and aero-sinusitis. *Laryngoscope, St. Louis,* 1943, *53:* 203–209. [R]

1854. Coronel, M. C. Las otitis medias. *Sanid. mil.,* 1949, *2:* 229–235. [D]

1855. Crowe, S. J. and E. W. Hagens. Otis media with effusion—challenge to otolaryngology. pp. 273–274 in: *The 1950 yearbook of the eye, ear, nose, and throat.* Chicago, The Year Book Publishers, Inc., 1951, 446 pp. [R]

1856. Dickinson, R. J. and C. A. Voelker. Aerosinusitus with hematoma. *U. S. Air Surg. Bull.,* 1945, *2:* 444. [CH]

1857. Dickson, E. D. D., J. E. G. McGibbon, and A. C. P. Campbell. Acute otitic barotrauma—clinical findings, mechanism and relationship to the pathological changes produced experimentally in the middle ears of cats by variations of pressure. pp. 60–83 in: *Contributions to aviation otolaryngology.* By E. D. D. Dickson. London, Headley Brothers, 1947, 257 pp. [R] [P]

1858. Dysart, B. R. Otitis media and complications. *Arch. Otolaryng., Chicago,* 1950, *51:* 106–123. [R]

1859. Eggston, A. A. and D. Wolff. Inflammation of the middle ear (otitis media). pp. 333–353 in: *Histopathology of the ear, nose, and throat.* Baltimore, The Williams & Wilkins Co., 1947, viii, 1080 pp.

1860. Gt. Brit. FPRC. Head measurements in cases of recurrent otitic baratrauma. *F. P. R. C. Rept. no. 608,* 6 February 1945, 4 pp. [P]

1861. Haines, H. L. and J. D. Harris. Aerotitis media in submariners. *J. industr. Hyg.,* 1947, *29:* abstract section: 40. *Ann. Otol., etc., St. Louis,* 1946, *55:* 347–371. [P]

1862. Harvey, W. Investigation and survey of malocclusion and ear symptoms, with particular reference to otitic barotrauma (pain in ears due to change in altitude). *Brit. dent. J.,* 1948, *85:* 219–225. [P]

1863. Hoilien, M. J. An improvement in technique of the Proetz method of treating paranasal sinusitis. *J. Aviat. Med.,* 1945, *16:* 358–359.

1864. Hollender, A. R. Purulent otitis media. pp. 513–534. in: *Office treatment of the nose, throat, and ear.* Chicago, The Year Book Publishers, Inc., 1950, 620 pp. [R]

1865. Jordan, R. Chronic secretory otitis media. *Laryngoscope, St. Louis,* 1949, *59:* 1002–1015.

1866. Kerekes, G. Y. Oto-rhinologiai tapasztalatok a Caisson-betegségnél. [Oto-rhinological experiences in caisson disease.] *Oto-rhino-laryng. Danub.,* 1948, *1:* 181. Abstr. [CH] [R]

1867. Lentine, J. A review of one hundred cases of acute aero-otitis. *Arch. Otolaryng., Chicago,* 1946, *43:* 293–297.

1868. Lieberman, A. T. Aero-otitis media in pressure chamber "flights". *Arch. Otolaryng., Chicago,* 1946, *43:* 500–508. [P]

1869. McGuckin, F. Chronic otitis media. *J. Laryng.,* 1949, *63:* 328–336.

1870. Morrison, W. W. Acute inflammation of the tympanic cavity and mastoid cells. pp. 107–134 in: *Diseases of the ear, nose, and throat.* New York, Appleton-Century-Crofts, Inc., 1948, 772 pp.

1871. Nielsen, J. C. Studies of the aetiology of acute otitis media. Copenhagen, Ejnar Munksgaard, 1945, 191 pp. [P, R]

1872. Ogden, F. W. A study of altitude chamber aero-otitis media. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 147, Rept. no. 1,* 5 May 1943, 6 pp.

1873. Ogden, F. W. Tubal resistance and aero-otitis media. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 268, Rept. no. 1,* 24 June 1944, 4 pp. [P]

1874. Patton, R. A. Purulent otitis media in albino rats susceptible to sound-induced seizures. *J. Psychol.,* 1947, *24:* 313–317.

1875. Saruwatari, Z. [Otitis media.] *Nippon rinsyo,* 1948, *6:* 127–130. (English pagination.)

1876. Shilling, C. W. Aero-otitis media and auditory acuity loss in submarine escape training. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–434 (Sub. no. 90), Rept. no. 1,* 8 October 1944, 8 pp. [CH]

1877. Shilling, C. W., H. L. Haines, J. D. Harris, and W. J. Kelly. Aerotitis media. A brief presentation of its symptomatology, prevention and treatment. *J. Aviat. Med.,* 1947, *18:* 48–55.

1878. Tauride, D. *Sumbole eis ten meses aerotitos (Spoude tesnosou epi toon hellenoon Iptamenoon).* [Contribution to the study of aero-otitis media. A study of the disease among flying personnel of the Royal Hellenic Air Force.] Thesis (Medecine), Athens, 1950, 105 pp.

1879. Teed, R. W. A contribution of war experience to the etiology of otitis media. *Trans. Amer. Acad. Ophthal. Oto-laryng.,* 1949, *53:* 254–260. [R]

1880. Tobey, H. G. Acute catarrhal otitis media with effusion. *Trans. Amer. otol. Soc.,* 1948, *36:* 51–71.

1881. Anon. Diver's ear (otitic barotrauma). *Roy. Nav. med. Bull.,* 1943, *5:* 13–14.

1882. Anon. Barotrauma. *Roy. Nav. med. Bull.,* 1946, *22:* 53–57. [R]

D. OTITIS MEDIA THERAPY

1. GENERAL CONSIDERATIONS

The following references are included as introductory source material of particular interest to the general reader and to those desiring brief reports on therapy of acute otitis media.

1883. Fox, S. A. The management of the acute ear. *Laryngoscope, St. Louis,* 1946, *56:* 312–319.

1884. Pompe, J. Otitis media acuta in njegova terapija. [Acute otitis media and its therapy.] *Med. Glasn.,* 1949, *3:* 102–107.

1885. Singleton, J. D. Acute otitis media; its management by the general practitioner and pediatrician. *J. Okla. med. Ass.,* 1946, *39:* 325–328.

1886. Trapasso, T. J. Aerotitis program in the Fifteenth Air Force. *Ann. Otol., etc., St. Louis,* 1945, *54:* 716–721.

2. USE OF VASOCONSTRICTOR AND ANALGESIC DRUGS

Ogden (*1887*) 1943 reported that the use of various vasoconstrictor sprays just prior to simulated flights in an altitude chamber did not reduce

the occurrence of aerotitis media to a degree considered statistically significant. However, in the group of subjects who had received tuamine (2-amino heptane sulphate) as a nasal spray, the total incidence of aerotitis media was definitely reduced. Reid (*1888*) 1946 has used ephedrine solutions instilled into the ear in the treatment of acute otitis media with advantage in early cases. Unger (*1889*) 1947 has described a process of cocainization of the tympanum via the Eustachian tube.

1887. Ogden, F. W. A study of the effects of vasoconstrictor solutions on altitude chamber aero-otitis media. U. S. NRC–CAM. *C. A. M. rept. no. 170,* 1 June 1943, 8 pp. [P]

1888. Reid, W. O. Treatment of acute otitis media by decongestion. *Brit. med. J.,* 1946, *1:* 648–649. [P]

1889. Unger, M. Cocainizing the tympanum via the eustachian tube. A new method. *Arch. Otolaryng., Chicago,* 1947, *45:* 693–696.

3. CHEMOTHERAPY

None of the references given below refers to aerotitis media incurred in military situations involving pressure changes. Most of them refer to acute or chronic otitis media with bacterial infection in which antibiotic treatment is indicated. These references are included because aerotitis media may be complicated by infection with suppuration, and in such cases or if such a condition is feared, recourse to antibiotics is indicated.

1890. Baba, S. Fundamental studies on the penicillin treatment of otitis media. *J. oto-rhinolaryng. Soc., Tokyo,* 1951, *54 (11):* (English text pagination), 53–54.

1891. Bateman, G. H. The place of chemotherapy and penicillin in the treatment of acute otitis media. *Irish J. med. Sci.,* 1947, 6th Series, 457–464.

1892. Belfort, F. Nova técnica de tratamento de otites médias agudas por meio de antibióticos. *Med. cir. pharm.,* 1950, 96–98.

1893. Crowe, S. J., W. E. Loch, and E. N. Broyles. Diseases of the ear, nose, and throat. *Ann. rev. Med.,* 1950, *1:* 339–354. [R]

1894. Evans, M. G. The treatment of acute suppurative otitis media. The relative merits of chemotherapy and myringotomy in avoiding surgical mastoiditis. *Ann. Otol. etc. St. Louis,* 1951, *60:* 638–647.

1895. Hétroy, M. Les sulfamides dans les otites aigües et subaigües. *Concours méd.,* 1946, *68:* 505. [D]

1896. House, H. P. Otitis media. A comparative study of the results obtained in therapy before and after the introduction of the sulfanomide compounds. *Arch. Otolaryng., Chicago,* 1946, *43:* 371–378.

1897. Ježek, K. Ambulantní léčba akutních otitid penicilinem. *Čas Lék. čes.,* 1951, *90:* 1128–1132. [D]

1898. Karatay, S. Treatment of otitis media and sinusitis with penicillin. *Arch. Otolaryng., Chicago,* 1947, *45:* 288–293.

1899. Kučera, M. Penicilin u akutních zánětů středoušních. [Penicillin and acute otitis media.] *Prakt. Lék., Praha,* 1948, *28:* 208–209.

1900. Landgren, N. Penicillinterapi vid akuta otiter. *Nord. Med. Stockholm,* 1949, *42:* 1401–1403. [CH]

1901. Monteiro, A. Sulfas e penicilina no tratamento das otites médias agudas e suas complicações. Estudo comparativo. *Hospital,* 1949, *36:* 23–53.

1902. Nielsen, J. C. Effect of dipencillin administered once daily on acute otitis media, with particular reference to the bacteriology. *Acta oto-laryng.,* 1951, *39:* 222–237. [CH]

1903. Ohsawa, R., and M. Kamata. A new form of chemotherapy in treatment of otitis media purulenta chronica. *J. oto-rhinolaryng. Soc., Tokyo,* 1950, *53 (8):* (Japanese text pagination), 265–267. (English text pagination), 28–29.

1904. Piquet, J. La sulfamidotherapie dans les otites aigües d'après les publications des auteurs nordiques. *Ann. Oto-laryng.,* 1946, *13:* 344–347. [D]

1905. Rajner, V. Příspěvek k léčbě akutních otitid penicilinem. *Čas Lék. čes.,* 1951, *90:* 1124–1128. [CH]

1906. Ramadier, J. A. A propos d'une série de deboires avec la sulfamido-penicillo thérapie dans le traitement des otites aigües. *Sem. Hôp., Paris,* 1947, *23:* 2579–2583. [CH]

1907. Reimann, H. A. Acute otitis media. pp. 1–293—1–294 in: *Treatment in general medicine.* Volume I. Fourth edition. Philadelphia, F. A. Davis Co., 1948, 780 pp.

1908. Riskaer, N. Penicillin treatment of simple acute otitis media. *Acta oto-laryng., Stockh.,* 1949, *37:* 230–238.

1909. Rodel, A. Zur Behandlung der akuten Mittelohrentzündungen mit Sulfonamiden. *Pract. oto-rhino-laryng.,* 1946, *8:* 499–504. [CH]

1910. Royal Society of Medicine, Section of otology. Society proceedings, 5 December 1947. Discussion on penicillin treatment in acute otitis media. *J. Laryng.,* 1948, *62:* 608–612.

1911. Salinger, A. Antibiotics in ear, nose, and throat. *Wis. med. J.,* 1948, *47:* 997–998.

1912. Simpson, J. F. Otorhinolaryngology. pp. 317–331 in: *Penicillin. Its practical application.* Edited by A. Fleming. London, Butterworth & Co., Ltd., 1950, 454 pp.

1913. Sobieski, J. Pénicillinothérapie locale des otites moyennes aigües. *Concours méd.,* 1949, *71:* 1193–1194. [CH]

1914. Tobey, H. G. The sulfonamide drugs in the treatment of acute otitis media. *Ann. Otol., etc., St. Louis,* 1942, *51:* 945–954.

1915. Vicencio, A. B. Treatment of chronic otitis media with a mixture of glycerite of hydrogen peroxide, streptomycin and penicillin. *Arch. Otolaryng., Chicago,* 1951, *53:* 87–88.

1916. Volkmar, E. Soll man bei der akuten otitis media Sulfonamide verordnen? *Med. Klinik.,* 1943, *43:* 390–391. [D]

1917. Weiss, J. A. Transtubal instillation of penicillin in acute otitis media. *Arch. Otolaryng., Chicago,* 1946, *43:* 17–18.

1918. Wilcox, J. G. Penicillin treatment of acute middle ear and mastoid infections. *Penn. med. J.,* 1947, *50:* 574–577. [CH]

1919. Wilson, C. P. Report of 110 cases of acute infection of the ear treated with penicillin. *J. Laryng.,* 1946, *61:* 404–410.

1920. Young, A. and I. S. Hall. Penicillin treatment in acute suppurative otitis media with special reference to long-term hearing. *J. Laryng.,* 1948, *62:* 551–556. [CH]

4. IRRADIATION THERAPY

Faulty opening of the mouth of the Eustachian tube, especially during compression, lies at the basis of aerotitis media. Lymphoid hyperplasia around the mouth of the tube is believed to be a cause of this defective function. Accordingly, a therapeutic and preventative procedure has been developed in which recession of the lymphoid tissue is effected by means of local irradiation. For this purpose, radium, radon, and X-rays have been utilized. Shilling, Haines, Harris, and Kelly (*1929*) 1946 have reported that the use of X-ray is of inconclusive value and has been discontinued. Other evidence indicates that the administration of X-ray therapy presents particular problems. The use of radium, however, has proved successful, according to the authors, in well over 90 percent of the cases.

Irradiation treatment has been widely employed in the U. S. Air Force and evaluations of results are given in the following references: *1921, 1923, 1924, 1925, 1926, 1930,* and *1931*. These reports indicate that irradiation is not a cure-all and will not affect symptoms having a functional basis. However, it appears that there is objective improvement in approximately 90 percent of cases (*1925, 1926*). For an anlysis of 28 failures out of 1,177 patients treated at the Third Air Force Irradiation Unit, a paper by Glauber, Smith, and Earl (*1924*) 1945 should be consulted.

The reader is advised to consult a carefully prepared report by Dickson and McGibbon (*1922*) 1949 for a cautionary and critical treatment of the subject of irradiation therapy for otitis media. The authors draw attention to the possible dangers of haphazard introduction of powerful sources of radio-activity into the nasopharynx. Positioning is of vital importance if the lymphoid tissue is actually to be affected. The authors pointed out in 1949 that at that time it was still too early to express any opinion as to the occurrence of delayed, local ill effects. The authors stated that in order to irradiate adequately the entire Eustachian tube from a single nasopharyngeal source, the dosage with radium would need to be such as would be dangerous to tissues adjacent to the source. It was considered consequently that deep X-irradiation was the only acceptable procedure. A safe method of application of X-irradiation was described which would not cause damage to the skin or tissues in the region of Eustacian tube. A disadvantage of X-irradiation is that a considerable volume of tissue must be irradiated.

1921. Collins, B. E., J. W. Eschenbrenner, Jr., and P. L. Lyle. Aerotitis and radium therapy in the Eighth Air Force. *Ann. Otol., etc., St. Louis,* 1945, *54:* 694–707.

1922. Dickson, E. D. D. and J. E. G. McGibbon. The treatment of recurrent otitic barotrauma by irradiation (with special reference to lymphoid tissue in the submucosa of the eustachian tube). *J. Laryng.,* 1949, *63:* 647–671.

1923. Fowler, E. P., Jr. Irradiation of the Eustachian tube. *Arch. Otolaryng., Chicago,* 1946, *43:* 1–11.

1924. Glauber, J. J., J. W. Smith, and D. H. Earl. Report of the Third Air Force irradiation unit, 31 August 1945. *Ann. Otol., etc., St. Louis,* 1945, *54:* 686–693.

1925. Hendricks, J. E. and A. T. Lieberman. Activities of the irradiation clinic at Westover Field, Massachusetts. *Ann. Otol., etc., St. Louis,* 1945, *54:* 662–683.

1926. Mikell, J. S. The use of radium in the aerotitis control program in the Twelfth Air Force. *Ann. Otol., etc., St. Louis,* 1945, *54:* 708–715.

1927. Northington, P. Radium therapy in aerotitis media. *Nav. med. Bull., Wash.,* 1946, *46:* 1559–1567. [M]

1928. Proctor, D. F. Irradiation for the elimination of nasopharyngeal lymphoid tissue. *Arch. Otolaryng., Chicago,* 1946, *43:* 473–480.

1929. Shilling, C. W., H. L. Haines, J. D. Harris, and W. J. Kelley. The prevention and treatment of aerotitis media. *Nav. med. Bull., Wash.,* 1946, *46:* 1529–1558. [P]

1930. Weymuller, E. A. and P. L. Magnuson. Report of 52 cases of recurrent aerotitis, First Air Force, Mitchel Field, New York. *Ann. Otol., etc., St. Louis,* 1945, *54:* 684–685.

1931. Anon. The use of radium in the aerotitis control program of the Army air forces. *Ann. Otol., etc., St. Louis,* 1945, *54:* 650–660.

5. DENTAL THERAPY

Kelly (*1932, 1933, 1934,* and *1935*) 1946 and Kelly and Langheinz (*1936*) 1946 have reported successful investigations of dental treatment for the prevention of aerotitis media. Success claimed earlier in relieving ear symptoms in aviators with over-closure of the mandible by inserting a splint between the back teeth to open the bite suggested to Kelly that the muscles concerned with the movement of the jaw are also in some way involved with the functions of the Eustachian tube. Kelly reasoned that abnormally strained muscular activity during jaw movement might exert a deleterious effect on the function of the Eustachian tube. Dental treatment was accordingly devised and carried out to correct occlusion and provide free movement of the mandible and normal unstrained muscle action during all jaw movements. Casts of the jaws were made and X-rays were taken in the open and closed positions, and points on the teeth which hampered excursions were corrected.

A group of 50 subjects with severe aerotitis media (*1936*) who demonstrated defective mandibular functions were selected for treatment of the occlusion defect. Following treatment, 46 of these patients were able to undergo pressure without otological symptoms or signs. These findings were based upon objective examination of each ear with the otoscope in the hands of an experienced oto-

laryngologist. Three out of the four unsuccessful cases responded to radium therapy. One case resisted all attempts at therapy. In explanation of the rationale of dental therapy in aerotitis media, the authors suggested that normally the action of the superior pharyngeal constrictor muscles stimulates the lymph vessels draining the Eustachian tube. Dysfunction of that muscle may lead to stasis of the tube. The action of the buccinator muscle is intimately interrelated with the action of the superior pharyngeal constrictor muscle through the pterygomandibular raphe, and it was argued that the rationale of dental therapy lay in restoring normal, unstrained function to the buccinator and hence to the superior pharyngeal constrictor muscle. This was believed to reduce an abnormal tourniquet effect of the latter upon the lymphatics and so restore the normal massaging effect, thereby stimulating lymphatic drainage and thus reducing congestion of the Eustachian tube. This theory of lymphatic stasis is substantiated by the fact that the amount of lymphoid tissue present in the nasopharynx has little bearing upon the success or failure of the dental method of treatment.

1932. Kelly, W. J. The results of dental therapy in 50 cases of aerotitis media in submarine personnel based upon a new functional concept of eustachian tube blockage. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–434 (Sub. no. 90), Interval report no. 1,* 21 January 1946, 15 pp. [P]

1933. Kelly, W. J. Dental treatment of trismus, tinnitus, otalgia and obscure neuralgias. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–434 (Sub. no. 90), Interval Report no. 2,* 31 January 1946, 17 pp.

1934. Kelly, W. J. A rapid dental treatment for the prevention of aerotitis media. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–434 (Sub. no. 90), Interval Report no. 3,* 1 February 1946, 11 pp. [CH]

1935. Kelly, W. J. An evaluation of a dynamic concept of dental treatment based upon a functional classification of malocclusion. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–434 (Sub. no. 90), Interval Report no. 4,* 15 February 1946, 10 pp.

1936. Kelly, W. J. and H. W. Langheinz. Dental treatment for the prevention of aerotitis media. *Ann. Otol., etc., St. Louis,* 1946, *55:* 13–28. [P]

6. SURGICAL AND PHYSICAL PROCEDURES

Various methods to inflate the middle ear and to facilitate drainage of fluid from the middle ear have been devised. These and other surgical procedures in otitis media are described in the references that follow.

1937. Daggett, W. I. Operative treatment of chronic suppurative otitis media. *J. Laryng.,* 1949, *63:* 635–646.

1938. Fowler, E. P. Treatment of otitis media. pp. 626–629 in: *The specialties in general practice.* Edited by Russell L. Cecil. Philadelphia, W. B. Saunders Co., 1951, 818 pp.

1939. Ogden, F. W. Modified Politzerization in treatment of aero-otitis media. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 173, Rept. no. 1,* 3 August 1943, 5 pp.

1940. Ogden, F. W. Continuous pressure politzerization in the prevention of altitude chamber aero-otitis media. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 177 Rept. no. 1,* 31 August 1943, 5 pp. [P]

1941. Olmsted, F. Modifications of a device for testing patency of the Eustachian tube. Rept. no. 53 in: *Studies in Aviation Medicine.* Yale aero-medical research unit, Yale University School of Medicine, New Haven, Conn., 1941–1946.

1942. Seltzer, A. P. Newly designed paracentesis needle for use in aerotitis media. *Arch. Otolaryng., Chicago,* 1951, *53:* 672–674.

1943. Trowbridge, B. C. A new treatment of acute aero-otitis media. *Arch. Otolaryng., Chicago,* 1949, *50:* 255–263. [CH]

1944. Unger, M. A new method of treatment for nasal sinusitis: oxygen inflation. *Arch. Otolaryng., Chicago,* 1945, *41:* 353–354. [M] [CH]

E. OTITIS EXTERNA

Otitis externa is a clinical entity with high morbidity in military personnel on tropical duty. It is also a condition to which underwater swimmers are subject unless effective preventive measures are taken. Otitis externa in underwater swimmers is discussed in the section on diseases prevalent in swimmers (p. 332). The causative organism may be any of a variety of bacteria and fungi. Ashley (*1945*) 1946 classifies the condition into three groups. In group I, the external auditory canal is moist and filled with exudate and debris. In group II, there is a cellulitis of the deep tissue of the canal. Group III cases are more chronic with persistent itching and other symptoms. Cases will occur under continuous exposure to hot, humid environments, especially after swimming or taking showers, unless care is taken to keep the ear canals dry. Most cases of bacterial otitis externa are considered to be caused by various species of the genus Pseudomonas (*1946, 1947, 1948, 1952, 1953,* and *1956*). The role of fungi in the etiology of otitis externa is believed by Syverton, Hess, Krafchuk, Josselyn, and Freyvogel (*1956*) 1946 to have been overemphasized, and Senturia (*1953*) 1945 states that fungi played little part in the inception or persistence of otitis externa seen at Randolph Field, Tex.

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1953. Senturia, B. H. Etiology of externa otitis. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 349, Rept. no. 1,* 15 January 1945, 15 pp.

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F. OTITIS EXTERNA THERAPY

Correct hygiene of the external ear is essential in preventing otitis externa. The canal should be kept clean and dry and free from moisture. Treatment is most successful, according to McLaurin (*1957*) 1951, when the otologist limits himself to a few antibacterial or fungicidal agents and supplements this treatment by thorough cleansing of the external auditory canal and by utilizing resources for the relief of discomfort. The use of "iso-par" ointment in the treatment of otitis externa in Okinawa in 1946 was described by Senturia (*1960*) 1946. Senturia and Broh-Kahn (*1961*) 1947 described the use of streptomycin locally in the form of an ointment in 54 patients with diffused otitis externa in the San Antonio area. These cases showed a high number of cultures of *Pseudomonas.* Successful treatment was accompanied by a rapid disappearance of *Pseudomonas* from infected ears. Treatment of otitis externa with 250 micrograms and 1 mg. of streptomycin per gram of ointment base was no more effective than treatment with the base alone. Treatment with 5 mg. of streptomycin per gram of ointment base gave beneficial results where simple cleansing of the ear canal and drying failed to produce favorable clinical effects. The use of various vehicles and antibiotics in the external auditory canal in the treatment of otitis externa has been discussed in detail in a report by Senturia and Doubly (*1962*) 1947. When both streptomycin and penicillin were incorporated in an aqueous vehicle, a potentiated antibiotic effect was obtained. This combination was valuable in mixed infections. Senturia and Wolf (*1963*) 1945 found that sulfanilamide had marked fungistatic effects when applied to the surface of cultures of a number of fungi. Sulfathiazole, sulfadiazine, sulfaguanidine, and sulfamerazine had no observable effect upon the growth of these fungi. The authors recommended local application of powdered sulfanilamide in cases of otomycocis. Sulfanilamide was found not to affect cultures of monilia. Local and systemic use of sulfonamides has also been discussed by Simon (*1964*) 1945, and Sullivan and Smith (*1965*) 1950.

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III. DECOMPRESSION SICKNESS

A. GENERAL CONSIDERATIONS

For a comprehensive review of the literature on decompression sickness up to 1 January 1946, reference should be made to appropriate sections (pp. 108–162) in the first volume of this Sourcebook. The references given below provide access to the general subject of decompression sickness as it has developed since the beginning of 1946. The reader will find especially helpful the reports by Behnke (*1968*) 1945, (*1969*) 1947, (*1970*) 1940, (*1971*) 1950, (*1972*) 1951; and Fulton (*1978*) 1948, (*1979*) 1951; and Fulton and Nims (*1980*) 1941–46.

The term "decompression sickness" refers to the signs, symptoms, and underlying pathological processes arising from rapid reduction of barometric pressure from high pressures to 1 atmosphere as in caisson work, tunneling operations, or in diving.

The term also covers the deleterious effects of decompression to levels of less than 1 atmosphere as experienced in high-altitude flights or in experimental decompression chambers. The symptoms include pain (bends), painful breathing (chokes), and paralysis. There may also be visual and other sensory disturbances, involvement of the integument, convulsive seizures and other central nervous symptoms, and even sudden death. Decompression sickness appears to have as its etiological basis the liberation of gas bubbles directly into various tissues or into the bloodstream in which they are carried to find lodgment in various parts of the body. Lesions may be found in the central nervous system, the eye, the internal ear, as well as in the bones and joints and other areas. The condition may be prevented by following appropriate decompression procedures breathing air or helium-oxygen mixtures. At safe depths not sufficient to cause oxygen intoxication, pure oxygen may be breathed during decompression. Treatment includes recompression in a pressure chamber to an appropriate depth with administration of oxygen down to 50 feet. Various special symptoms and signs require special treatment. The acute symptoms are usually transient and there is ordinarily no permanent damage, providing recompression treatment has been carried out adequately. However, chronic disturbances following repeated decompression over the years may supervene. Chronic lesions of the bone and joints, for example, may be due to this cause.

1966. Alpers, B. J. Caisson disease. pp. 311–312 in: *Clinical neurology.* Second edition. Philadelphia, F. A. Davis Co., 1949, 846 pp.

1967. Antunez, Nieto. Efectos del aumento de la presion. El mal del buzo. pp. 117–118 in: *Higiene naval y nociones de anatomia y fisiologia.* Moret, La Coruna, 1950, 321 pp.

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1969. Behnke, A. R. A review of physiologic and clinical data pertaining to decompression sickness. U. S. Navy. NMRI. *Project X–443, Rept. no. 4,* 13 May 1947, 35 pp. [R]

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1988. Anon. Decompression sickness. *J. Amer. med. Ass.*, 1946, *130:* 82. [R]

B. CLINICAL PICTURE OF DECOMPRESSION SICKNESS

The recent literature does not add any essentially new contribution to knowledge of the actual symptomatology of decompression sickness beyond that set forth on pages 115 to 137 of the first volume of this Sourcebook. Of the references given below, items *1989, 1993,* and *1996* describe the clinical picture of decompression sickness following decompression from pressures higher than 1 atmosphere. References *1990, 1991, 1992, 1994, 1995, 1997, 1998, 1999,* and *2000* describe the symptomatology of decompression sickness as encountered in rapid ascent to altitude.

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1994. Hartrijsen, F. B. Tarmgas og hoydeflyging. [Intestinal gas and high altitude flying.] *Nord. Med., Stockholm,* 1949, *42:* 1319–1321.

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1999. Tobias, C. A. Decompression sickness in actual flights. pp. 360–377 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Subcommittee on decompression sickness, National Research Council, Philadelphia, W. B. Saunders Co., 1951, 437 pp. [CH] [D]

2000. Whitten, R. H. Scotoma as a complication of decompression sickness. *J. industr. Hyg.*, 1947, *29:* abstract section: 82. *Arch. Ophthal., Chicago,* 1946, *36:* 220–224. [P]

C. CASE REPORTS

A large number of case histories of decompression sickness are referred to on pages 121 to 137 of the first volume of this Sourcebook. Reference should be made to these histories for basic information on the clinical pattern of decompression sickness. The references listed below report specific cases of decompression sickness due to decompression from high pressures as well as decompression to altitude or simulated altitude.

Van Der Aue (*2011*) 1948 reported a case of decompression sickness in a diver aboard the U. S. S. *Chanticleer.* The diver descended to 356 feet, remained there for 10 minutes, and ascended to 50 feet without symptoms. After completing the 60-foot stop and the 50-foot stop he breathed oxygen. He was then asked to unshackle and reported that he had done so. Mumbling sounds then ensued and at 30 feet, telephone contact was lost. When the diver was brought to the surface he was found to be unconscious and suffering convulsive body movements. The face was pink, the body was limp. He was carried to a recompression chamber in his diving suit and was recompressed to a simulated level of 165 feet 6 minutes later. He began thrashing about and required restraint. He was unconscious for 29 minutes. Table 2A was used for decompression. On regaining consciousness the diver was mildly disoriented and complained of headache and soreness in the ears. There was some bleeding from the mouth. At the simulated 40-foot level, otoscopic examination revealed hemorrhagic eardrums, but no perforations. Some blood streaked the posterior pharyngeal wall. This blood probably came from the Eustachian tubes or the nasal sinuses. The patient said he remembered nothing after he unshackled. The patient had never before experienced any symptoms.

A case history is described by van Keuren (*2012*) 1946 of decompression sickness in a diver attached to the U. S. S. *Coucal.* The U. S. S. *Coucal* was anchored for diving activity 12 miles from Pearl Harbor. Lead-line soundings indicated a depth of 130 feet. Divers overside were paid out 200 feet of hose on air. After 4 minutes on the bottom, the diver started up according to the standard table for air dives. Pain was experienced in the chest at 10 feet, and the diver was brought to the surface and recompressed in the chamber on the ship. Complete relief was experienced at 30 feet. Two or three minutes after treatment, the diver noted a tingling

sensation in the left leg, but nevertheless went to chow. The condition became more serious and weakness developed. The diver was put back into the chamber 42 minutes after the onset of symptoms and was taken to a simulated depth of 165 feet where he remained for 20 minutes. During the first hour of treatment, the weakness rapidly increased until the diver was unable to walk, stand, or crawl. When the ship reached dock, a medical examination revealed impaired touch and pain perception from the level of the umbilicus downward. There was weakness of lower back movements and weakness of motion in the right hip, knee, ankle, and toes, and complete inability to move the left hip, knee, ankle, and toes. Position sense was normal. The superficial abdominal and cremasteric reflexes were absent bilaterally. The patellar, knee, and ankle jerks were hyperactive and bilaterally equal. The Babinski reflex was positive on both sides. There was mild clonus on the left ankle. Pinprick perception was impaired, but not absent from the level of the 10th thoracic segment downward. It was considered that bubbles had lodged in the anterior horn of the spinal cord at about the level of the 10th thoracic segment and had been there for 40 minutes before treatment was begun. Apparent progression of the symptoms was considered possibly due to nerve injury already done, plus involvement of a surrounding area by edema and hemorrhage. As to further treatment, oxygen was given but was stopped because of increased nervousness and finger twitchings. Helium-oxygen mixtures and air were alternated every half hour. The following morning a small amount of urine was passed and catheterization was done. Later, the deep reflexes in the lower extremities became depressed and disappeared. Subsequently the patient was left with residual symptoms and was surveyed from the naval service. This case stresses the importance of immediate recompression to an adequate depth.

Welham and Waite (*2013*) 1951 reported two unusual cases of decompression sickness. The first was a 21-year-old diver who reported to the diving school with complaint of pain, weakness, and numbness of the right upper arm and shoulder, and mottling of the entire right arm. The last dive had been made 36 hours prior to the onset of symptoms. The dive had been made to 25 to 35 feet in the Anacostia River. The patient had been recompressed with relief at 20 feet and surfaced several minutes later, but the symptoms had returned 1 hour subsequently. The patient was recompressed according to table I of the treatment tables in the U. S. Navy Diving Manual and surfaced symptom free. The second case was that of a 24-year-old student diver who made a dive to 27 feet for 96 minutes and who 7 hours later suffered a sharp pain in the wrist. Hot soaks at home brought no relief. Chamber recompression gave relief at 56 feet. This patient was treated according to table I and surfaced symptom free. Twenty-one hours after initial treatment, the patient again complained of pain in the affected area. When no relief was afforded at 165 feet, the case was determined not to be bends. X-ray investigation at the U. S. Naval Hospital at Bethesda revealed no fracture, and the final diagnosis was that of a sprain.

Two further cases of decompression sickness in divers are given by Laane (*2004*) 1949 and Bayulkem and Akyol (*2001*) 1950. Parodi (*2010*) 1948 has presented five cases of decompression sickness in caisson workers who experienced acute pain in the extremities and abdomen, vertigo, and general malaise.

For reports of cases of decompression sickness due to high altitude or simulated high altitude, the following references are given: *2002, 2003, 2005, 2006, 2007, 2008,* and *2009.*

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2010. Parodi, V. M. Rilievi semeiologici e clinici nelle forme osteomioartralgiche della malattia dei cassoni. *Med. d. Lavoro,* 1948, *39:* 73–79. [CH]

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D. INCIDENCE, DIAGNOSIS, AND PROGNOSIS OF DECOMPRESSION SICKNESS

The references given below are principally concerned with altitude decompression sickness. However, they are included because they provide useful source material for the reader who is concerned with factors affecting incidence and prognosis of decompression sickness.

2014. Allan, J. H. Traumatic calcifications: a precipitating factor in "bends" pain. *J. industr. Hyg.*, 1946, *28:* Abstract section: 47. [CH]

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2016. Anthony, R. A., R. W. Clarke, A. Liberman, L. F. Nims, J. Tepperman, and S. M. Wesley. Effects of local compression, impairment of venous return and arterial tournequet upon the intensity of established "Bends" pain. U. S. NRC–CAM. *C. A. M. Rept. no. 143,* 16 June 1943, 6 pp.

2017. Bierman, H. R. The relationship of age to the incidence of decompression in aviation. U. S. Navy. NATC., Pensacola, Fla. School of aviation medicine. *Project X–10 (Av–R7–1)*, 13 July 1943, 5 pp. [P]

2018. Burkhardt, W. L., H. F. Adler, A. F. Thometz, A. J. Atkinson, and A. C. Ivy. Decompression sickness: some factors which affect the incidence of bends at altitude. *J. industr. Hyg.*, 1947, *29:* abstract section: 58. *J. Amer. med. Ass.*, 1947, *133:* 373–377.

2019. Burkhardt, W. L., A. F. Thometz, and A. C. Ivy. The effect of deliberate hyperventilation on the incidence of "intolerable" cases of bends and chokes. U. S. NRC–CAM. *C. A. M. Rept. no. 438,* June 1945, 4 pp.

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2023. Gray, J. S. Aeroembolism induced by exercise in cadets at 23,000 feet. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 227, Rept. no. 1,* 26 January 1944, 3 pp. [P]

2024. Gray, J. S. Constitutional factors affecting susceptibility to decompression sickness. pp. 182–191 in: *Decompression sickness. Caisson sickness, diver's and flier's bends, and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [D]

2025. Griffin, D. R., S. Robinson, H. S. Belding, R. C. Darling, and E. Turrell. The effects of cold and rate of ascent on aero-embolism. U. S. NRC–CAM. *C. A. M. Rept. no. 174,* 22 June 1943, 12 pp. [P]

2026. Griffin, D. R., S. Robinson, H. S. Belding, R. C. Darling, and E. S. Turrell. The effects of cold and rate of ascent on aero-embolism. *J. Aviat. Med.*, 1946, *17:* 56–66.

2027. Hodes, R. and M. G. Larrabee. The relation between alveolar carbon dioxide tension and susceptibility to decompression sickness. *Amer. J. Physiol.*, 1946, *147:* 603–615. [P]

2028. Henry, F. M. The role of exercise in altitude pain. U. S. NRC–CAM. *OEMcmr–196, Rept. no. 460,* September 1945, 2 pp. Abstr.

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2036. Rodbard, S. Recurrence of decompression sickness on reascent to high altitude. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 59–60. *J. industr. Hyg.*, 1948, *30:* abstract section: 19. [P]

2037. Smedal, H. A. and E. B. Brown, Jr. Incidence of bends pain in a short exposure to simulated altitudes of 26,000, 28,000, and 30,000 feet. U. S. Navy, NATC., Pensacola, Fla. School of aviation medicine. *Project X–609 (Av–311–h)*, 1 September 1945, 8 pp. [P]

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E. ETIOLOGY OF DECOMPRESSION SICKNESS

Catchpole and Gersh (*2043*) 1947 and Gersh and Catchpole (*2046*) 1951 have pointed out that the evidence is overwhelming that gas bubbles are the primary pathogenic agent in decompression sickness, whether due to decompression from high-pressure atmospheres or decompression to altitude. The authors believe that the gas bubbles are chiefly intravascular and these are held to be responsible for nearly all important phases of the syndrome of decompression sickness. Extravascular gas bubbles are also believed to occur under certain circumstances in decompression from high-pressure atmospheres, but they are restricted to certain lipid-rich structures. The pathological effects may be vastly greater after decompression from high-pressure atmospheres than at altitude. Bean (*2042*) 1950 considers that extravascular bubble formation is more important because there is no local cyanosis, pallor, or cooling to implicate defective blood supply. Also, he points out that X-rays reveal no consistent vascular distribution of bubbles. Bean accepts the possibility that intravascular bubbles may accentuate focal changes. Intravascular bubbles are found in divers dying with bends or in the vena cava of decompressed animals. He considers that intravascular bubbles may be secondary and arise after symptoms occur. He states that bubbles may go on forming after death. He considers that the weight of evidence supports the secondary formation of intravenous bubbles in animals after stasis or stagnation following vasospasm.

Nims (*2053*) 1947 and (*2054*) 1951 has propounded a physical theory of decompression sickness. Gas bubbles growing in tissues must displace and deform adjacent structures. If the deformation pressure exceeds a threshold value, nerve fibers or endings are stimulated by the mechanical deformation of the tissues. Decompression sickness pain is stated not to differ in kind from the pain produced by excessive stretching of the eardrum or the pain due to unequalized pressure in the sinuses. Reduction of the deformation pressure to below threshold values provides immediate relief of painful stimuli. It is not the size of the bubble that determines the appearance of the symptons, but rather the magnitude of the distortion pressure that is produced. Nims believes that bends pain comes from extravascular bubbles because reascent to altitude produces pain in exactly the same area as before. When the deformation pressure is near threshold value, a slight increase in carbon dioxide level or nitrogen in diving could well be the critical determinant in decompression sickness.

For other studies relating to the etiology of decompression sickness, particularly at altitude, the following references may be consulted: *2041, 2044, 2045, 2047, 2048, 2049, 2050, 2051, 2052, 2055, 2056, 2057, 2058,* and *2059.*

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2044. Clarke, R. W., A. M. Liberman, L. F. Nims, J. Nyboer, and J. Tepperman. Peripheral circulation during decompression—digital volume-pulse. U. S. NRC–CAM. *C. A. M. rept. no. 232,* 29 November 1943, 4 pp.

2045. Ferris, E. B., Jr. and G. L. Engel. The clinical nature of high altitude decompression sickness. With a note on psychologic reactions by J. Romano. pp. 4–52 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [R]

2046. Gersh, I. and H. Catchpole. Decompression sickness: physical factors and pathologic consequences. pp. 165–181 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [D]

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2049. Knisely, M. H., S. Gray, H. M. Peck, R. L. Nichols, L. Warner, J. A. Orcutt, and N. Anderson. A brief review of some of the evidences indicating the necessity for controlling the circulatory homeo-static reactions of decompressed men. *Appendix II* in Methods and testing of therapeutic agents in relation to bends by M. H. Knisely. U. S. NRC–CAM. *OEMcmr–290, C. A. M. rept. no. 473,* September, 1945, 13 pp.

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2051. Lund, D. W. and J. H. Lawrence. An hypothesis as to a cause of "bends" pain with observations on massage at high altitude. U. S. NRC–CAM. *C. A. M. rept. no. 404,* 10 January 1945, 9 pp. [M]

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2053. Nims, L. F. A physical theory of decompression sickness. Yale University, New Haven, Conn. Aeromedical research unit. *Rept. no. 55, Contract N6–ori–44, T. O. VII,* 1 May 1947, 27 pp.

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2055. Patek, P. R., A. Lazarow, E. Bartosh, and G. H. Scott. Observations on living periosteum and peritoneum at simulated high altitudes. U. S. NRC–CAM. *C. A. M. rept. no. 244,* 17 January 1944, 3 pp. [P]

2056. Sureda, F. L. Effets des changements de pression atmosphérique sur l'organisme humain. *Bull. int. Serv. Santé Arm.*, 1946, *19:* 180–182.

2057. Swindle, P. F. The possible relationship between intravascular agglutination of erythrocytes and decompression sickness. U. S. NRC–CAM. *C. A. M. rept. no. 178,* 13 August 1943, 8 pp. [P]

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2059. Tobias, C. A., W. F. Loomis, and J. H. Lawrence. Studies on skin temperature and circulation in decompression sickness. *Amer. J. Physiol.*, **1947,** ***149:*** **626–633.** [P]

F. PATHOLOGICAL LESIONS

For a detailed description of pathological lesions encountered in decompression sickness, the appropriate section (pp. 142–162) in the first volume of this Sourcebook should be consulted. The literature that has appeared since the first volume was published has been mainly concerned with bone and joint lesions. With more effective modern treatment of acute symptoms, it would appear that lesions of the central nervous system, and visual and auditory apparatus, are less common than previously. Fewer cases are now being reported with serious, obvious neurological and other sequelae. On the other hand, chronic bone and joint lesions detected in caisson workers and divers, often many years after exposure to decompression, have caused interest and aroused concern. Improved radiological techniques have made possible the more accurate and detailed study of these lesions, and considerations of workmen's compensation renders important an accurate evaluation of their relationship to exposure to decompression. Often bone and joint symptoms are complained of by former divers and caisson workers who give no history of episodes of severe decompression sickness. It is possible that lesions in bones or joints may follow even a single attack of decompression sickness, provided it is of sufficient intensity.

For review articles on bone and joint lesions due to decompression sickness, references by the following may be consulted: Brailsford (*2062*) 1948, Geschickter and Copeland (*2064*) 1949, Pugh (*2079*) 1951, Mouchet and Mouchet (*2076*) 1941, Nicoulaud (*2078*) 1940, and Raymond (*2080*) 1948. The bone and joint lesions are characterized by multiple areas of localized necrosis in the bone and joint surfaces and are believed to be the result of air emboli (*2062* and *2064*). Examination of persons who work in compressed air shows a high incidence of skeletal lesions (*2079*). These are often extensive and multiple, and in some instances are bilateral. As mentioned above, they often occur in divers or caisson workers who have never had symptoms of bends. Their high incidence in divers and caisson workers leaves little doubt in the mind of Pugh (*2079*) that they are the direct result of exposure to decompression. The lesions are most frequently found in the long bones, usually of the lower extremity. Hands and feet are spared. The lesions involve the distal ends of the shaft and perhaps the epiphyseal portion of the bone. At first, the lesion consists merely of a region of rarefaction which represents an aseptic necrosis of the cancellous portion of the bone. As healing takes place, there is replacement of the necrotic bone by new bone which is irregular in architecture and is of greater density than normal. The lesion is often well circumscribed from the surrounding normal bone by a zone of calcification and ossification at the periphery of the lesion. In some cases, the central portion remains rarefied, but usually the entire lesion becomes irregularly calcified. When the end of the bone is affected, the changes are greater than those involving the diaphysis. Aseptic necrosis involves the articular surface and is accompanied by devitalization of the articular cartilage. Infarction through the articular surface takes place, and the surface becomes irregular and rough. The bone beneath the articular surface becomes rarefied in places with spotty zones of increased density. As revascularization occurs, the affected bone becomes more rarefied and is abnormally soft so that, with weight bearing, deformity results. The final appearance in a weight-bearing joint is one of secondary osteoarthritis. Because the lesions are often symmetrical it is only by the recognition of areas of old diaphyseal infarction or knowledge that the patient has been a caisson worker or diver that the changes in the joint can be distinguished from primary osteoarthritis.

A number of case histories are given in which bone and joint complications were significant. In 1941, de La Marnierre (*2069*) reported three cases

with bony and articular complications. The first case was that of a 26-year-old man who had been working in caissons for 3 years. He complained of pain in his limbs half an hour after leaving the chamber. He returned some months later with pain and partial immobilization of his legs. When examined in the hospital about a year later, he still showed limitation of movement of the left leg. X-ray revealed clearly a necrosis at the level of the inferior part of the head of the femur. A second X-ray taken 3 years subsequently showed extension of the lesion. The second case is that of a man of 42 who had worked in caissons since 1938 and who presented himself to the clinic with painful rheumatism. In 1939, after working for 5 hours in a caisson, he developed symptoms half an hour after decompression. These included vertigo, excessive perspiration, and pain in the legs, particularly the hip. The patient returned to work in 15 hours. Six months later, he returned after having been injured by a winch. The pain of the left thigh persisted. On examination about 18 months later, the patient was walking with difficulty. There was limitation in the movement of the hip joint. X-rays revealed chronic lesions of the head of the left femur. The third case was that of a 42-year-old man who had worked in caissons for 2 years. In June 1939, he had a violent crisis with pain in the legs, more accentuated in the lower left leg, thigh, hip, and elbow. The pain appeared 2½ hours after leaving the chamber. One month later, he was still complaining of pain in the left hip region. The lesions appeared in the superior part of the head of the femur.

Wertheimer and Mansuy (*2082*) 1941–42 reported the case of a 34-year-old patient who appeared for the first time in the hospital for an abscess of the right big toe. The patient returned 2 years later, suffering from a painful toe with ulceration. X-rays showed arthritic lesions and the toe was amputated. On return to the hospital 6 months later, the patient had a pain in his left hip. He stated that he had had hip pain 8 years previously after exposure to decompression in caissons. There was no history of syncope, abdominal pain, respiratory symptoms, or hemorrhages. The patient had blamed the pain on the caisson work and had stopped work 3 months after the onset of the symptoms. On examination, there was a limitation of movement of the left hip and X-rays showed a considerable deformity of the head of the femur, the internal part being very dense and compact. The articular areas were deformed. Osteophytes were seen at the inferior part of the articulation.

Guillain and Crossiord (*2065*) 1943 reported the case of a 34-year-old patient who presented himself to the clinic in 1940 with a history of having worked in a caisson for 3 years. On his first trip into the caisson he worked for 8 hours at 2½ atmospheres. On decompression he was surfaced too rapidly and bled through the nose and ears. One-half hour after coming out of the caisson he had extreme pain in his extremities, particularly in the shoulders. The patient complained of insomnia and joint pain. The patient was seen 8 months later with pain in the right shoulder and left tibia, and soon after with pain in the opposite members. Six months subsequently, he was seen again and was unable to work. Examination 4 months later revealed further limitation of joint movement. X-rays of the glenoid fossa and surrounding bone showed pathological changes. The inferior part of the articulation appeared healthy, but the superior part was nipped and there was bony erosion. The head of the humerus was flattened and atrophied. The lesions in this case were not attributed to gaseous arterial embolism but to liberation of gas bubbles in the bone marrow. Such bubbles may be liberated, according to authors, in a region of poor circulation, diminishing the chance of resorption and producing a necrotic lesion.

Mazel and Bourret (*2071*) 1945 have listed 2 case histories, one a man of 33 and the other of 34. In both of these cases, X-rays revealed decalcified areas in the bone. Fischgold, Coville, and Doassans (*2063*) 1948 presented a case in which radiological evidence of alterations in osseous tissue was obtained 2 years after the decompression sickness episode.

For other studies of pathological lesions in decompression sickness, the reference list below may be consulted.

2060. Alamercery, D. *Les ostéo-arthropathies des ouvriers travaillant dans les caissons à air comprimé.* Thèse (méd.) Lyon, Bosc and Riou, 1945, 60 pp. *Arch. mal. prof.*, 1946, *7:* 317–318. Abstr.

2061. Bourret, J., P. Fraisse, and H. Fraisse. La maladie des caissons: contribution à l'étude des lesions ostéo-articulaires des tubistes. *Arch. mal. prof.*, 1948, *9:* 309–311. [CH]

2062. Brailsford, J. F. Caisson disease. pp. 648–649 in: *The radiology of bones and joints.* Baltimore, Williams & Wilkins Co., 1948, 760 pp. [D]

2063. Fischgold, H., R. Coville, and P. Doassans. Altération chronique des épiphyses dans la maladie des caissons. *J. Radiol. Electrol.*, 1948, *29:* 230–231. [CH]

2064. Genschickter, C. F. and M. M. Copeland. Caisson disease. p. 783 in: *Tumors of bone.* Philadelphia, J. B. Lippincott, 1949, 810 pp. [D]

2065. Guillain, G. and A. Grossiord. L'ostéo-arthrite de la "maladie des caissons." *Paris méd.*, 1943, *33:* 329–333. [CH]

2066. Hare, C. C. Compressed air illness (Caisson disease). pp. 675–680 in: *Injuries of the brain and spinal cord and their coverings.* Edited by Samuel Brock. Third edition. Baltimore, Williams & Wilkins Co., 1949, 783 pp.

2067. Haymaker, W. and C. Davison. Fatalities resulting from exposure to simulated high altitudes in decompression chambers. A clinicopathologic study of five cases. *J. Neuropath. exp. Neurol.*, 1950, *9:* 29–56. *Abstr. World Med.*, 1950, *8:* 93. [CH]

2068. Herget, ( ). Gelenkveranderungen bei Tauchern. *Klin. Wschr.*, 1948, *26:* 288. [CH]

2069. La Marnierre, P. de. and A. Salaun. Complications osseuses et articulaires de la maladie des caissons. *J. Chir., Paris*, 1941, *57:* 40–49. [R] [CH]

2070. La Marnierre, P. de. and A. Salaun. A propos des lésions ostéo-articulaires de la maladie des caissons. *Pr. méd.*, 1944, *52:* 248–249. [CH]

2071. Mazel, P. and J. Bourret. Ostéo-arthropathies consécutives au travail dans l'air comprimé. *J. méd. Lyon*, 1945, *26:* 55–61. [CH]

2072. Michelis, F. de. Lee altarazioni dell'apparato masticatorio nei lavatori dei cassoni. *Rass. med. indust.*, 1951, *20:* 151–158.

2073. Molfino, F. Contributo alla diagnostica differenziale dell'osteoartrosi cronica da malattia dei cassoni. *Rass. med. indust.*, 1950, *19:* 274–275.

2074. Molfino, F. Contribution au diagnostic différentiel de l'ostéoarthrite chronique, conséquence de la maladie des caissons. *Arch. mal. prof.*, 1951, *12:* 271–274. [CH]

2075. Molfino, F. and G. Balestra. L'ostéonécrose aseptique et l'ostéorthrose de la maladie des caisson. *Arch. mal. prof.*, 1950, *11:* 411–412. Abstr. [D]

2076. Mouchet, A., and A. Mouchet. Les lésions des os et des articulations dans la "maladie de caissons." *Pr. méd.*, 1941, *49:* 670–673. [R]

2077. Nicolas, M. Notions nouvelles sur la maladie de l'air comprimé et son traitement dans le travail en tube caissons. *Méd. usine.*, 1949, *11:* 321–328. *Arch. mal. prof.*, 1950, *11:* 411. Abstr. [D]

2078. Nicoulaud, M. D. M. La maladie des caissons a forme d'arthrite de la hanche. Thèse (méd.), Paris, 1940, 75 pp.

2079. Pugh, D. G. Caisson disease. pp. 227–230 in: *Roentgenologic diagnosis of diseases of bones.* New York, Thomas Nelson and Sons, 1951, 316 pp. [D]

2080. Raymond, M. V. Les ostéo-arthrites pneumatiques. Lésions osseuses des tubistes et des scaphandriers. *Arch. mal. prof.*, 1948, *9:* 437–442. [R]

2081. Thomas, S. F. and O. L. Williams. High-altitude joint pains (bends): their roentgenographic aspects. *Radiology*, 1945, *44:* 259–261.

2082. Wetheimer, P. and L. Mansuy. Troubles trophiques des orteils, arthrite chronique de la hanche et maladie des caisson. *Lyon chir.*, 1941–1942, *37:* 26–29. [CH]

G. PREVENTION AND TREATMENT OF DECOMPRESSION SICKNESS, INCLUDING PRESELECTION TESTS

1. GENERAL STUDIES

A comprehensive review of the literature dealing with prevention and treatment of decompression sickness up to 1 January 1946 is to be found on pages 260 to 300 of the first volume of this Sourcebook. The sections that follow in the present volume are not designed to reevaluate the material already published in the first volume but are planned to provide a guide to newer literature. For general considerations of prevention and treatment, references *2084, 2085,* and *2086* are especially useful.

2083. Gray, J. S. The effects of pressure breathing on decompression sickness and circulatory reaction in cadets. U. S. AAF. Randolph Field, Tex., School of aviation medicine. *Project 248, Rept. no. 1,* 15 March 1944, 8 pp. [P]

2084. Huston, J. W. and W. J. Alexander. Diving at U. S. Naval Torpedo Station, Newport, R. I. *Nav. med. Bull., Wash.*, 1946, *46:* 348–352.

2085. U. S. Navy. BuMed. Deep-sea diving. pp. 213–226 in: *A manual of naval hygiene.* Washington, D. C., Government Printing Office, 1943, 340 pp.

2086. U. S. Navy. BuNavPers. Lecture on (B) compressed air illness. pp. 74–80 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp. [D]

2. DECOMPRESSION PROCEDURES

The reader may consult references *2089* and *2090* for description of the decompression tables in use in the U. S. Navy. Figure 1 reproduces the decompression table for air dives taken from the U. S. Navy Diving Manual 1943 which is in current use. This figure gives depths from 40 feet to 300 feet for various exposure times in minutes. For each particular depth at a given time from leaving the surface to beginning of ascent, stops at different depths in minutes are set forth.

Surface decompression is also described in items *2089* and *2090,* and Van Der Aue, Kellar, Brinton, Barron, Gilliam, and Jones (*2091*) 1951 have reported calculations and tests of decompression tables for air dives employing the procedure of surface decompression and the use of oxygen. These authors point out that the average total times of decompression using tables which they have derived is about 45 percent less than that necessary with the current air surface decompression procedure. Oxygen was administered at 40 feet instead of 50 feet because of some cases of nausea. In many instances, bends symptoms would rapidly disappear when the diver was recompressed to 40 feet to receive oxygen decompression only to reappear or lead to additional symptoms after final decompression was completed. This was attributed to "silent" bubble formation which occurs as a result of a supersaturation of the tissues during this critical period of the dive. The authors therefore recommended a recalculation to correct defective tables using decompression ratios which offer deeper and longer water stops (see fig. 2).

For British (*2087*), French (*2088*), and Swedish (*2092*) comments on decompression procedures, papers by Davidson, Sutton, and Taylor (*2087*) 1950; Tailliez, Dumas, Cousteau, Alinat, and Devilla (*2088*) 1949; and von Döbeln (*2092*) 1948 should be consulted.

Figure 1.—Decompression table (Air) (U. S. Navy Diving Manual—1943).

Depth up to—	Time from leaving surface to beginning of ascent	Stop at different depths in minutes		
Feet	Minutes	30′	20′	10′
40	120	...	...	0
40	180	...	...	2
40	240*	...	...	4
40	300	...	...	6
50	78	...	...	0
50	120	...	...	2
50	150	...	...	5
50	190*	...	...	9
50	300	...	...	12
60	55	...	...	0
60	75	...	...	2
60	110	...	...	13
60	150*	...	5	15
60	180	...	7	16
60	210	...	8	18
70	43	...	...	0
70	60	...	...	4
70	75	...	...	13
70	90	...	4	16
70	120*	...	13	16
70	150	...	18	21
70	180	...	21	32
80	35	...	...	0
80	50	...	...	6
80	70	...	6	16
80	100	...	20	16
80	115*	...	22	26
80	150	...	28	29
90	30	...	...	0
90	45	...	...	6
90	60	...	9	16
90	75	...	18	14
90	95*	2	27	21
90	130	9	27	29

Depth up to—	Time from leaving surface to beginning of ascent	Stop at different depths in minutes			
Feet	Minutes	40′	30′	20′	10′
100	25	...	...	...	0
100	40	...	...	...	12
100	60	...	...	18	16
100	75	...	...	27	21
100	85*	...	6	28	21
100	90	...	8	27	24
100	120	...	17	28	48
110	20	...	...	...	0
110	35	...	...	...	12
110	55	...	...	22	21
110	75*	...	14	27	37
110	105	2	22	29	50
120	18	...	...	...	0
120	30	...	...	...	11
120	45	...	...	18	21
120	65*	...	13	28	32
120	100	5	22	27	69
130	15	...	...	...	0
130	35	...	...	11	15
130	52	...	6	28	28
130	60*	...	13	28	28
130	90	9	22	28	69
140	15	...	...	...	4
140	30	...	...	8	21
140	45	...	5	27	27
140	55*	...	15	28	32
140	85	14	22	32	69
150	15	...	...	...	7
150	30	...	...	13	21
150	38	...	...	28	30
150	50*	...	16	28	32
150	80	18	23	32	68

Depth up to—	Time from leaving surface to beginning of ascent	Stop at different depths in minutes								
Feet	Minutes	90′	80′	70′	60′	50′	40′	30′	20′	10′
160	15	...	...	...	...	...	...	...	...	9
160	34	...	...	...	...	...	...	...	27	28
160	45*	...	...	...	...	...	...	17	28	43
160	75	...	...	...	...	3	19	23	34	68
170	15	...	...	...	...	...	...	...	...	11
170	30	...	...	...	...	...	...	...	24	27
170	40*	...	...	...	...	...	...	19	28	46
170	75	...	...	...	...	9	19	23	38	68
185	15	...	...	...	...	...	...	...	...	25
185	26	...	...	...	...	...	...	...	24	37
185	35*	...	...	...	...	...	...	19	28	46
185	65	...	...	...	18	18	23	37	65	51
200	15	...	...	...	...	...	...	...	...	32
200	23	...	...	...	...	...	...	...	23	37
200	35*	...	...	...	...	...	...	22	28	46
200	60	...	...	5	18	18	23	37	65	51
210	15	...	...	...	...	...	...	...	...	35
210	30*	...	...	...	...	...	5	16	28	40
210	55	...	...	6	18	18	23	37	65	51
225	15	...	...	...	...	...	...	...	6	35
225	27*	...	...	...	...	...	22	26	35	48
225	60	...	...	13	18	18	23	47	65	83
250	15	...	...	...	...	...	...	...	17	37
250	25*	...	...	...	...	2	23	26	35	51
250	50	...	12	14	17	19	29	49	65	83
300	12	...	...	...	...	...	...	...	20	37
300	20	...	...	...	...	9	23	26	35	51
300	45	6	14	15	17	18	31	49	65	83

Note.—*Optimum exposure time.
Rate of ascent not to exceed 25 feet per minute.

Figure 2.—Surface decompression table using oxygen.

1** Depth in feet	2** Time	3** Time (min.) at water stops breathing air at— 60′	50′	40′	30′	4** Surface Interval Not To Exceed 5 Minutes	5** Time (min.) at 40′chamber stop oxygen	6** 2-Minute Ascent From 40 Feet in Chamber to Surface While Breathing Oxygen	7** Approximate total decompression time (min.)
70	52	0	0	0	0		0		3
70	90	0	0	0	0		15		24
*70	120	0	0	0	0		23		32
70	150	0	0	0	0		31		40
70	180	0	0	0	0		39		48
80	40	0	0	0	0		0		3
80	70	0	0	0	0		14		23
80	85	0	0	0	0		20		29
80	100	0	0	0	0		26		35
*80	115	0	0	0	0		31		40
80	130	0	0	0	0		37		46
80	150	0	0	0	0		44		53
90	32	0	0	0	0		0		4
90	60	0	0	0	0		14		24
90	70	0	0	0	0		20		30
90	80	0	0	0	0		25		35
*90	90	0	0	0	0		30		40
90	100	0	0	0	0		34		44
90	110	0	0	0	0		39		49
90	120	0	0	0	0		43		53
90	130	0	0	0	0		48		58
100	26	0	0	0	0		0		4
100	50	0	0	0	0		14		24
100	60	0	0	0	0		20		30
100	70	0	0	0	0		26		36
*100	80	0	0	0	0		32		42
100	90	0	0	0	0		38		48
100	100	0	0	0	0		44		54
100	110	0	0	0	0		49		59
100	120	0	0	0	3		53		66
110	22	0	0	0	0		0		5
110	40	0	0	0	0		12		23
110	50	0	0	0	0		19		30
110	60	0	0	0	0		26		37
*110	70	0	0	0	0		33		44
110	80	0	0	0	1		40		52
110	90	0	0	0	2		46		59
110	100	0	0	0	5		51		67
110	110	0	0	0	12		54		77
120	18	0	0	0	0		0		5
120	30	0	0	0	0		9		20
120	40	0	0	0	0		16		27
120	50	0	0	0	0		24		35
*120	60	0	0	0	2		32		45

1** Depth in feet	2** Time	3** Time (min.) at water stops breathing air at— 60′	50′	40′	30′	4** Surface Interval Not To Exceed 5 Minutes	5** Time (min.) at 40′chamber stop oxygen	6** 2-Minute Ascent From 40 Feet in Chamber to Surface While Breathing Oxygen	7** Approximate total decompression time (min.)
120	70	0	0	0	4		39		54
120	80	0	0	0	5		46		62
120	90	0	0	3	0		51		72
120	100	0	0	6	15		54		86
130	15	0	0	0	0		7		5
130	30	0	0	0	0		12		23
130	40	0	0	0	0		21		32
130	50	0	0	0	3		29		43
*130	60	0	0	0	5		37		53
130	70	0	0	0	7		45		63
130	80	0	0	6	7		51		76
130	90	0	0	10	12		56		90
140	13	0	0	0	0		0		6
140	25	0	0	0	0		11		23
140	30	0	0	0	0		15		27
140	35	0	0	0	0		20		32
140	40	0	0	0	2		24		38
140	45	0	0	0	4		29		45
140	50	0	0	0	6		33		51
*140	55	0	0	0	7		38		57
140	60	0	0	0	8		43		63
140	65	0	0	3	7		48		70
140	70	0	2	7	7		51		80
150	11	0	0	0	0		0		6
150	25	0	0	0	0		13		25
150	30	0	0	0	0		18		30
150	35	0	0	0	4		23		39
150	40	0	0	3	6		27		49
150	45	0	0	5	7		33		58
*150	50	0	2	5	8		38		66
150	55	2	5	9	4		44		78
160	9	0	0	0	0		0		7
160	20	0	0	0	0		11		24
160	25	0	0	0	0		16		29
160	30	0	0	0	2		21		35
160	35	0	0	4	6		26		49
160	40	0	3	5	8		32		62
*160	45	3	4	8	6		38		73
170	7	0	0	0	0		0		7
170	20	0	0	0	0		13		26
170	25	0	0	0	0		19		32
170	30	0	0	3	5		23		44
170	35	0	4	4	7		29		58
*170	40	4	4	8	6		36		73

*These are the optimum exposure times for each depth which represent the best balance between length of work period, safety and amount of useful work for the average diver. Exposure beyond these times is permitted only under special conditions.

**Notes on columns.

Column 1. Depth—In feet, gage (art. 836).

Column 2. Time—Interval from leaving the surface to leaving the bottom.

Column 3. Water stops—Time spent at tabulated stops using air. If no water stops are required, use a 25-foot-per-minute rate of ascent to the surface. When water stops are required use a 25-foot-per-minute rate of ascent to first stop. Take an additional minute between stops. Use 1 minute for the ascent from 30 feet to the surface.

Column 4. Surface interval—The surface interval shall not exceed 5 minutes and is composed of the following elements:

(a) Time of ascent from the 30-foot water stop, or from 30 feet if no water stops are necessary, to the surface (1 minute).

(b) Time on surface for landing the diver on deck and undressing (not to exceed 3½ minutes).

(c) Time of descent in the recompression chamber from the surface to 40 feet (about ½ minute).

Column 5. During the period while breathing oxygen, the chamber shall be ventilated as outlined in article 674.

Column 6. Surfacing—Oxygen breathing during this 2-minute period shall follow the period of oxygen breathing tabulated in column 5 without interruption.

Column 7. Total decompression time—This includes—

(a) Time of ascent from bottom to first stop, or to 30 feet if no water stop is required, at 25 feet per minute.

(b) Sum of tabulated water stops, column 2.

(c) 1 minute between water stops.

(d) Surface interval.

(e) Time at 40 feet in recompression chamber, column 4.

(f) Time of ascent, an additional 2 minutes, from 40 feet in the recompression chamber to the surface, column 5.

The approximate Total Decompression Time may be shortened only be decreasing the time required to undress the diver on deck.

2087. Davidson, W. M., B. M. Sutton, and H. J. Taylor. Investigation into the decompression tables. Report I. Decompression ratio for goats following long exposure and return to atmospheric pressure without stoppages. Appendix "A" by Case, R. A. M. Statistical analysis of the site of bends. Gt. Brit. RNPRC–MRC, UPS. *R. N. P. 50/582, U. P. S. 110, D. P. 2,* February 1950, 12 pp. [P]

2088. Tailliez, P., F. Dumas, J. Y. Cousteau, J. Alinat, and F. Devilla. Tables de plongée du G. R. S. pp. 97–108 in: *La plongée en scaphandre.* Paris, Elzevir, 1949, 119 pp.

2089. U. S. Navy. BuNavPers. Lectures on (A) decompression tables. pp. 69–74 in: *Submarine medicine practice. Nav Pers 10838,* March 1949, 182 pp. [D]

2090. U. S. Navy. BuShips. Decompression tables. pp. 78–81 in: *Chapter 94. Salvage section II. Diving.* 25 January 1951, U. S. Government printing office, Washington, D. C., 1951, 93 pp.

2091. Van Der Aue, O. E., R. J. Kellar, E. S. Brinton, G. Barron, H. D. Gilliam, R. J. Jones. Calculation and testing of decompression tables for air dives employing the procedure of surface decompression and the use of oxygen. U. S. Navy. Naval gun factory, EDU. *Project NM 002 007, Rept. no. 1,* November 1951, 52 pp. [M] [P]

2092. Döbeln, W., von. Surface decompression in deep diving. *Acta physiol. scand.,* suppl., 1948, *53:* 17.

2093. Yarbrough, O. D. Calculation of decompression tables. U. S. Navy. Naval gun factory, EDU. No date, 46 pp.

3. HELIUM-OXYGEN ADMINISTRATION

Effect of respiratory gas density on resistance to respiratory gas flow in man has been investigated by Otis and Bembower (*2103a*) 1951. A comparison was made of the resistance to the respiratory gas flow in man breathing air, or an 80 percent helium-20 percent oxygen mixture, or oxygen in a low-pressure chamber at equivalent altitudes of 18,000 and 36,000 feet. The results indicate that less alveolar pressure is required to produce a given velocity of gas flow when a person breathes the helium mixture at altitude than when he breathes air at ground level. Theoretical treatment of the data indicates that this effect is due to a decreased turbulence with the less dense gas. Specht, Marshall, and Spicknell (*2104*) 1950 have indicated that with helium-oxygen mixtures, respiratory flow is facilitated.

Since an 80 percent helium-20 percent oxygen mixture is less dense than air or pure oxygen, it has been used in the treatment of asthma. Doll (*2098*) 1946 has reported the use of the helium-oxygen mixture in six cases of mild to severe asthma. Two of these patients were unable to tolerate respiration of the mixture through a B. L. B. mask. In the rest of the patients some improvement was noted comparable to that obtained from 100 percent oxygen. The author considered that helium was not likely to be of great value in asthma, where the obstruction is in the smallest respiratory passages and where it is probable that at least part of the increased respiratory effort is due to changes in tissue elasticity. Where respiratory obstruction exists in larger passages, there are good theoretical grounds, supported by experimental evidence, for expecting relief with helium.

For information on the thermodynamic properties of helium, a report by Norris and Akin (*2103*) 1947 may be consulted. The effect of helium on gas exchange of mice has been discussed by Cook, South, and Young (*2096*) 1951. Greenspan (*2099*) 1949 and (*2100*) 1950 has reported on the velocity and attenuation of sound in rarefied helium.

The rationale for the use of helium-oxygen mixtures in diving has been given on page 295 of the first volume of this Sourcebook. Consolazio (*2095*) 1948 has reported an economical and uniform method of mixing oxygen and helium for diving use. Molumphy (*2101* and *2102*) 1950 has given tables for helium-oxygen decompression. In order to reduce the incidence of oxygen intoxication, the oxygen stops have been moved up to 50 and 40 feet. Time to all stops for various depth dives and duration has been computed. Tests of the helium-oxygen diving tables have been reported by Van Der Aue, Molumphy, Tacke, and Blockwick (*2106*) 1949. Blockwick (*2094*) 1951 has given a detailed review of helium-oxygen diving. He points out that dives in excess of 150 feet on air are unsatisfactory because of the impairment of the mental processes of the diver. This anesthetic effect is caused by the high partial pressure of nitrogen. A helium-oxygen mixture is an excellent breathing medium for dives to greater depths because the mental facilities are practically unimpaired. To keep the carbon dioxide concentration within acceptable limits, a ventilation rate of 1.5 to 4.0 cubic feet per minute is necessary. Provision of this amount of gas is impractical and expensive. This problem was partially solved by the use of a carbon dioxide absorbent used in conjunction with a venturi recirculating system which permitted the gas to be used over again. This system was limited to 350 feet because at greater depths the carbon dioxide exceeded 3 percent effective. The solution to this problem was the improvement of the efficiency of the recirculating system. It was found that the new circulating system reduced the effective carbon dioxide concentration by 43 percent. Dives have been made to 561 feet with the new venturi recirculating system with good results.

For further reports on helium-oxygen diving, the following references may be consulted: *2097* and *2105.*

2094. Blockwick, T. N. *Helium-oxygen diving and the evaluation, redesign and testing of the helium-oxygen recirculating system.* Thesis, (Eng.), University of Maryland, June 1951, 73 pp.

2095. Consolazio, W. V. Preparation of compressed helium-oxygen gas mixtures. U. S. Navy. NMRI. *Project NM 011 015, Rept. no. 3,* 17 January 1948, 11 pp.

2096. Cook, S. F., F. E. South, Jr., and D. R. Young. Effect of helium on gas exchange of mice. *Amer. J. Physiol.,* 1951, *164:* 248–250. [P]

2097. Davis, R. H. Helium and oxygen in deep diving. The United States Navy oxy-helium tables. pp. 180–196 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press, Ltd., 1951, 670 pp. [D]

2098. Doll, R. Helium in the treatment of asthma. *Thorax,* 1946, *1:* 30–38.

2099. Greenspan, M. Attenuation of sound in rarefied helium. *Physiol. Rev.,* 1949, *75:* 197–198.

2100. Greenspan, M. Propagation of sound in rarefied helium. *J. acoust. Soc. Amer.,* 1950, *22:* 568–571.

2101. Molumphy, G. G. Computation of helium-oxygen decompression tables. U. S. Navy. Naval gun factory, EDU. *Project NS 186–201, Sub-task 4, Rept. no. 7–50,* 25 September 1950, 25 pp. [P]

2102. Molumphy, G. G. HeO_2 decompression tables. U. S. Navy. Naval gun factory, EDU. *Project NS–186–201, Sub-task 4, Rept. no. 8–50.* 26 September 1950, 26 pp.

2103. Norris, R. H. and S. W. Akin. Thermal conductivity and viscosity of helium, supplement to the main report entitled "The thermodynamic properties of helium at high pressures and temperatures." U. S. General Electric Company, Schenectady, N. Y. General Engineering and Consulting Laboratory, *Rept. no. 55141*—supplement, for Project Hermes, U. S. Army Ordnance, July 1947, 5 pp.

2104. Specht, H., L. H. Marshall, and B. H. Spicknall. Effects of helium and altitude on respiratory flow patterns. *J. appl. Physiol.,* 1950, *2:* 363–372.

2105. U. S. Navy. BuNavPers. Medical aspects and decompression procedures of diving with helium-oxygen. pp. 103–117 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp. [D]

2106. Van der Aue, O. E., G. G. Molumphy, A. W. Tacke, and T. N. Blockwick. Tests of present HeO_2 tables, the determination of CO_2 and O_2 percentages at various stages of the dives and the comparison of the present venturi recirculation system with the revised type with special regard to the effective CO_2 concentration at depths ranging from atmospheric to 429′. U. S. Navy. Naval gun factory, EDU. *Project NS 186–026, Rept. no. 13–49,* 12 December 1949, 16 pp.

4. HYDROGEN-OXYGEN ADMINISTRATION

Zetterström (*2108*) 1948 has devised an ingenious method of diving with a gas mixture containing hydrogen instead of helium. This hydrogen must be mixed with oxygen in a proportion in which the partial pressure of oxygen will be sufficient for breathing. However, the gas mixture must be safe from explosion. It will not explode if the oxygen content is less than 4 percent, regardless of the hydrogen or nitrogen content. If the gas mixture contains 4 percent oxygen, the partial pressure of the oxygen will not suffice until a depth of 30 meters or more has been reached. The diver must descend to 30 meters with ordinary air and then change to the hydrogen-oxygen mixture. So as to have sufficient quantities of gases, these must be manufactured aboard the vessel. By an ammonia-cracking process, a gas mixture containing 75 percent hydrogen and 25 percent nitrogen can be evolved. By adding 4 percent oxygen to the mixture, the final composition of the resulting gas will be 72 percent hydrogen, 24 percent nitrogen, and 4 percent oxygen. The author used the gas mixture in dives to 40 meters, 110 meters, and 160 meters. It was found at 110 meters that respiratory resistance was small and the narcotic effect of nitrogen negligible. An evaluation of hydrogen-oxygen diving in the prevention of decompression sickness and nitrogen narcosis has been given by Bjurstedt and Severin (*2107*) 1948.

2107. Bjurstedt, H. and G. Severin. The prevention of decompression sickness and nitrogen narcosis by the use of hydrogen as a substitute for nitrogen (the Arne Zetterstrom Method for deep-sea diving). *Milit. Surg.,* 1948, *103:* 107–116.

2108. Zetterstrom, A. Deep-sea diving with synthetic gas mixtures. *Milit. Surg.,* 1948, *103:* 104–106. *J. industr. Hyg.,* 1949, *31:* abstract section: 23–24.

5. OXYGEN ADMINISTRATION

Preoxygenation has been shown to be valuable in the prevention of decompression sickness in flying and in decompression chambers. Breathing oxygen acts by washing out nitrogen from the body. The following references on this topic have been selected: *2110, 2114, 2115, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2132, 2135,* and *2139.* It has also been found that oxygen inhalation reduces abdominal distension in flying by removal of nitrogen from the alimentary tract.

For further studies on the physiological effects of oxygen, the references given below may be consulted.

2109. Alella, A. and E. Meda. Frequenza cardiaca durante la respirazione di O_2 nell' uomo ed importanza del vago. *Boll. Soc. ital. Biol. sper.,* 1948, *24:* 581–582.

2110. Bateman, J. B . Review of data on value of preoxygenation in prevention of decompression sickness. pp. 242–277 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [D]

2111. Berger, L. B. and S. J. Davenport. Effects of the inhalation of oxygen. U. S. Bureau of mines. *Information circular 7575,* July 1950, 36 pp. [R]

2112. Beznak, A. B. L. and G. Liljestrand. The effect of variations in oxygen tension on the lymph flow. *Acta physiol. scand.,* 1949, *19:* 170–186. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1075.

2113. Campbell, A. and E. P. Poulton. Decompression after deep-sea diving. pp. 45–46 in: *Oxygen and carbon dioxide therapy.* London, Oxford University Press, 1938, 202 pp.

2114. Clarke, R. W., F. D. Humm, and L. F. Nims. The efficacy of preoxygenation in the prevention of decompression sickness. U. S. NRC–CAM. *C. A. M. rept. no. 31,* 4 November 1944, 5 pp.

2115. Clarke, R. W., F. D. Humm, and L. F. Nims. The efficacy of preflight denitrogenation in the prevention of decompression sickness. U. S. NRC–CAM. *OEMcmr–38, C. A. M. rept. no. 472,* 5 September 1945, 13 pp.

2116. Comroe, J. H. and P. Walker. Normal human arterial oxygen saturation determined by equilibration with 100 percent O_2 in vivo and by the oximeter. *Amer. J. Physiol.,* 1948, *152:* 365–371. [P]

2117. Fasciolo, J. C. and H. Chiodi. Arterial oxygen pressure during pure O_2 breathing. *Amer. J. Physiol.,* 1946, *147:* 54–65. [P]

2118. Fowler, W. S. and J. H. Comroe, Jr. The rate of increase of arterial oxygen saturation following inspiration of 100 percent oxygen. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 104. [P]

2119. Fowler, W. S. and J. H. Comroe, Jr. Lung function studies. I. The rate of increase of arterial oxygen saturation during the inhalation of 100 percent O_2 *J. clin. Invest.,* 1948, *27:* 327–334. [P]

2120. Gray, J. S. The effect of varying periods of denitrogenation on aeroembolism in cadets. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 164, Rept. no. 1,* 17 June 1943, 7 pp. [P]

2121. Gray, J. S. The effect of varying periods of denitrogenation on aeroembolism in cadets. U. S. NRC–CAM. *C. A. M. rept. no. 168,* 17 June 1943, 7 pp. [P]

2122. Gray, J. S. Effect of denitrogenation at various altitudes on aeroembolism in cadets. U. S. NRC–CAM. *C. A. M. rept. no. 258,* 5 January 1944, 7 pp.

2123. Gray, J. S. and S. C. F. Mahady. The prevention of aeroembolism in cadets at 45,000 feet by denitrogenation. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 252, Rept. no. 1,* 29 March 1944, 7 pp. [P]

2124. Gray, J. S., S. C. F. Mahady, and R. L. Masland. Studies on altitude decompression sickness. III. The effects of denitrogenation. *J. Aviat. Med.,* 1946, *17:* 606–610. [P]

2125. Henry, F. M. and S. F. Cook. Effectiveness of pre-flight oxygen breathing in preventing decompression sickness. *J. Aviat. Med.,* 1945, *16:* 350–355. [P]

2126. Henry, F. M., S. F. Cook, E. Strajman, and D. W. Lund. Effectiveness of preflight oxygen breathing in preventing decompression sickness. U. S. NRC–CAM, *C. A. M. rept. no. 384,* 30 October 1944, 17 pp.

2127. Jones, H. B. Preoxygenation and the rate of nitrogen elimination with regard to decompression sickness. U. S. NRC–CAM. OEMcmr–196, *C. A. M. rept. no. 491,* October 1945, 3 pp. [P]

2128. Karel, L. and R. E. Weston. Femoral arterial and venous blood nitrogen content of dogs during denitrogenation by continuous oxygen inhalation. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 342–343. [P]

2129. Karel, L. and R. E. Weston. Nitrogen content of femoral arterial and venous blood in anesthetized dogs denitrogenated by continuous inhalation of 99.6 percent oxygen. *Amer. J. Physiol.,* 1947, *151:* 71–79.

2120. Kline, R. F. Effects of severe anoxia and their amelioration. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 143–144.

2131. Linde Air Products Company. *Bibliography on oxygen therapy.* Revised edition. Linde Air Products Co., New York, N. Y., 1947, 99 pp. [B]

2132. McGoldrick, T. A., J. F. Lally, and L. L. Largby. Influence of demand and air dilutor demand oxygen systems used from sea level on the incidence of bends. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project X–201 (Av–R6–6), Rept. no. 1,* 2 November 1943, 3 pp. [P]

2133. Meda, A. and A. Allella. Diminuzione del volume-minuto nella respirazione di oxygen. Richerche nell'uomo. *Boll. Soc. ital. Biol. sper.,* 1948, *24:* 492–493.

2134. Miller, A. T., Jr. The influence of oxygen administration on the cardiovascular response to exercise. *Fed. Proc. Amer. Soc. exp. Biol.,* 1948, *7:* 81. [P]

2135. Murray, G. D. Effect of preoxygenation on resistance to decompression illness. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project X–141 (Av–R6–4),* 26 March 1943, 7 pp. [P]

2136. Nahas, G. G. and E. H. Morgan. Direct measurements of alveolar-arterial differences in oxygen tension in man breathing 100% oxygen. *Fed. Proc. Amer. Soc. exp. Biol.,* 1951, *10:* 96.

2137. Pogrund, R. S. and F. R. Steggerda. Studies on the removal of gas from the colon by oxygen inhalation. *J. industr. Hyg.,* 1949, *31:* abstract section: 84–85. [P]

2138. Preston, S. N. and N. K. Ordway. Observations of arterial oxygen content in children during the inhalation of air and 100 percent oxygen. *Amer. J. Physiol.,* 1948, *152:* 696–702. [P]

2139. Weston, R. E. and L. Karel. The influence of denitrogenation on the response of anesthetized dogs to intravenously injected oxygen. *J. clin. Invest.,* 1947, *26:* 837–848. [P]

6. RECOMPRESSION TREATMENT AND PROCEDURES

For basic information on the treatment of decompression sickness by recompression, papers by the following should be consulted: U. S. Navy, BuShips (*2140*) 1951, Van Der Aue, Duffner, and Behnke (*2141*) 1947, and Van Der Aue, Hayter, Brinton, Kellar, and Behnke (*2142*) 1945.

In figure 3 are given the treatment tables for use in the recompression treatment of caisson disease and air embolism. The figure shows in tables 1 and 1A the decompression schedule in the case of those suffering with bends pain in which the pain is relieved at recompression depths less than 66 feet. Tables 2 and 2A (of fig. 3) are used if the pain is relieved at recompression depths greater than 66 feet. If pain does not improve within 30 minutes at 165 feet, the case is probably not bends. The victim should be decompressed on table 2 or 2A. Table 3 and table 4 (of fig. 3) are for use with serious symptoms, including unconsciousness, convulsions, weakness, or inability to use the arms or legs, any visual disturbances, dizziness, loss of speech or hearing, or severe shortness of breath or chokes. Table 3

(of fig. 3) gives the decompression schedule in those cases where the symptoms are relieved within 30 minutes at 165 feet. Table 4 (of fig. 3) is used in those cases where the symptoms are not relieved within 30 minutes at 165 feet. If the symptoms return while breathing air during treatment with any of the tables given, the victim is to be recompressed to the depth of relief, but never less than a depth of 30 feet and then is to be decompressed from this depth according to table 4. If symptoms reoccur following treatment with any of the tables given in figure 3, the diver is to be recompressed to a depth giving relief. If relief occurs at depths less than 30 feet, the diver is to be taken to 30 feet and decompressed from the 30-foot stop to the surface according to table 3 in figure 3. If relief occurs deeper than 30 feet, the diver is to be retained at the depth of relief for 30 minutes and then is to complete the remaining stops of table 3 of figure 3, using air throughout.

Figure 3.—Treatment of caisson disease and air embolism (U. S. Navy Diving Manual—1952).

Stops		Bends—Pain only				Serious symptoms	
Rate of *Descent*—25 ft. per min. Rate of *Ascent*—1 minute between stops.		Pain relieved at depths *less than* 66 ft. Use Table 1–A if °2 is not available.		Pain relieved at depths *greater than* 66 ft. Use Table 2–A if °2 is not available. If pain does not improve within 30 min. at 165 ft., the case is probably *not* bends. Decompress on Table 2 or 2–A.		Serious symptoms include any one of the following: 1. Unconsciousness. 2. Convulsions. 3. Weakness or inability ot use arms or legs. 4. Any visual disturbances. 5. Dizziness. 6. Loss of speech or hearing. 7. Severe shortness of breath or chokes.	
						Symptoms *relieved* within 30 minutes at 165 ft. Use Table 3.	Symptoms *not relieved* within 30 minutes at 165 ft. Use Table 4.
Lbs.	Ft.	Table 1	Table 1–A	Table 2	Table 2–A	Table 3	Table 4
73.4	165			30 (Air)	30 (Air)	30 (Air)	30 to 120 (Air).
62.3	140			12 (Air)	12 (Air)	12 (Air)	30 (Air).
53.4	120			12 (Air)	12 (Air)	12 (Air)	30 (Air).
44.5	100	30 (Air)	30 (Air)	12 (Air)	12 (Air)	12 (Air)	30 (Air).
35.6	80	12 (Air)	12 (Air)	12 (Air)	12 (Air)	12 (Air)	30 (Air).
26.7	60	30 (°2)*	30 (Air)	30 (°2)*	30 (Air)	30 (°2)* or (Air)	6 hrs. (Air).
22.3	50	30 (°2)*	30 (Air)	30 (°2)*	30 (Air)	30 (°2)* or (Air)	6 hrs. (Air).
17.8	40	30 (°2)	30 (Air)	30 (°2)	30 (Air)	30 (°2) or (Air)	6 hrs. (Air).
13.4	30		60 (Air)	60 (°2)	2 hrs. (Air)	12 hrs. (Air)	First 11 hrs. (Air), then 1 hr. (°2) or (Air).
8.9	20	5 (°2)	60 (Air)		2 hrs. (Air)	2 hrs. (Air)	First 1 hr. (Air), then 1 hr. (°2) or (Air).
4.5	10		2 hrs. (Air)	5 (°2)	4 hrs. (Air)	2 hrs. (Air)	First 1 hr. (Air), then 1 hr. (°2) or (Air).
Surface			1 min. (Air)		1 min. (Air)	1 min. (Air)	1 min. (°2).

TIME AT ALL STOPS IN MINUTES UNLESS OTHERWISE INDICATED

If symptoms return while breathing air *during* treatment with any of the above tables, recompress to depth of relief but never less than a depth of 30 ft., and then complete decompression from this depth according to Table 4.

Some prime considerations in the recompression treatment of decompression sickness may be given. Experience has shown that failure to give treatment in doubtful cases is a frequent and important error. Another frequent error consists in delaying the recompression procedure. It has been found in the past that the longer the delay the deeper the diver will have to be taken for relief of symptoms. Failure to treat the serious cases adequately according to table 3 or 4 of figure 3 is a serious error. In all cases, the treated diver should be kept near the chamber for a 24-hour period in case symptoms return.

Bends symptoms may occasionally become temporarily worse if pressure is applied too rapidly. If this occurs, compression should be stopped momentarily and the pressure then slowly raised at a rate which the diver can tolerate. In all cases, particularly in serious cases with paralysis, the ability of the diver to stand up and walk the length of the chamber should always be tested. This test should be made routinely before the diver leaves the depth of relief of symptoms and also at the completion of the 30-foot stops. Additional treatment of bends symptoms includes first-aid measures. The patient should be lying down during the treatment to prevent, if possible, the movement of bubbles up into the brain. Again, it should be stressed that on the completion of treatment, the diver patient should always be kept near the chamber for not less than 24 hours in order to treat any recurrences immediately. When oxygen is administered in the treatment of decompression sickness, a fire hazard is always present. Smoking is prohibited and the chamber should be ventilated frequently to keep the oxygen concentration low. The highest concentration of oxygen, preferably above 95 percent, should be delivered to the diver patient. The mask should be leakproof in order to make treatment tables effective in the cases where oxygen is used. If possible, the oxygen should be humidified to avoid dryness of the nose and throat. Personnel giving treatment for recompression sickness using oxygen should always be conscious of the possible development of oxygen intoxication. At maximum pressures of treatment, helium-oxygen mixtures (about 80-to-20 ratio) may be used to advantage instead of air in all types of treatment.

Tenders must always be present in the chamber with divers breathing oxygen. Tenders require 60 minutes of oxygen during the last 60 minutes of the oxygen-therapy period outlined in tables 1 and 2 of figure 3. If the diver is treated as outlined in tables 3 and 4 of figure 3, the tender will necessarily be subjected to the same treatment. Decompression for additional tenders who may subsequently enter the decompression chamber for short periods will be carried out in accordance with the standard diving tables.

2140. U. S. Navy. BuShips. Compressed air illness and treatment tables. pp. 81–85 in: *Chapter 94. Salvage section II. Diving.* U. S. Government Printing Office, Washington, D. C., 25 January 1951, 93 pp.

2141. Van Der Aue, O. E., G. J. Duffner, and A. R. Behnke. The treatment of decompression sickness: an analysis of one hundred and thirteen cases. *J. industr. Hyg.*, 1947, *29:* 359–366.

2142. Van Der Aue, O. E., W. A. White, Jr., R. Hayter, E. S. Brinton, R. J. Kellar, and A. R. Behnke. Physiological factors underlying the prevention and treatment of decompression sickness. U. S. Navy. NMRI. *Project X–443, Rept. no. 1,* 26 April 1945, 12 pp.

7. DRUGS IN PREVENTION AND TREATMENT OF DECOMPRESSION SICKNESS

During World War II, investigations were conducted to evaluate the use of various drugs in the prevention and relief of pain and other symptoms of decompression sickness. Such studies were virtually limited to decompression sickness of altitude. The references given below indicate the trends of these studies.

2143. Comroe, J. H., Jr. The use of morphine and demerol for the relief of pain of bends. U. S. NRC–CAM. *C. A. M. rept. no. 198,* September 1943, 6 pp. [P]

2144. Ivy, A. C., A. J. Atkinson, H. Adler, and W. Burkhardt. Pertaining to the effect of B2B (dextro-amphetamine) and of preoxygenation plus B2B on the incidence of "bends" and "incapacitating bends and chokes" at 40,000 ft. for 1 hour. U. S. NRC–CAM. *C. A. M. rept. no. 113,* 23 December 1942, 4 pp. [P]

2145. Knisely, M. H. Methods and testing of therapeutic agents in relation to bends. U. S. NRC–CAM. *OEMcmr–290, C. A. M. rept. no. 473,* September 1945, 8 pp. [R] [P]

2146. Knisely, M. H., S. Gray, H. M. Peck, R. L. Nichols, L. Warner, and J. A. Orcutt. Specific individual controls for some types of decompression experiments on human subjects. U. S. NRC–CAM. *C. A. M. rept. no. 194,* 1 October 1943, 1 p. [P]

2147. Knisely, M. H., S. Gray, H. M. Peck, R. L. Nichols, L. Warner, J. A. Orcutt, and N. Anderson. Preliminary tests of the effect of intravenous aminophyllin in preventing or alleviating bends and chokes. U. S. NRC–CAM. *C. A. M. rept. no. 195,* 1 October 1943, 7 pp. [P]

2148. Ryder, H. W., G. L. Engel, J. Romano, J. P. Webb, M. A. Blankenhorn, E. B. Ferris, and W. E. Brown. An assay of dextro-amphetamine for its protective value in decompression sickness. U. S. NRC–CAM. *C. A. M. rept. no. 112,* 28 January 1943, 6 pp. [P]

2149. Williams, O. L., W. R. Lyons, E. V. Bridge, and S. F. Cook. The use of drugs for the prevention of decompression sickness. *J. Aviat. Med.*, 1946, *17:* 602–605. [P]

8. PRESELECTION TESTS

As indicated in the references given below (*2150–2171*), much time and effort has been expended on methods and procedures of evaluating differences

in susceptibility to decompression sickness due to high altitude. Preselection tests have been devised by the use of which the incidence of decompression sickness in a preselected group of men is less than the incidence in an unselected group. The exact incidence in the selected group depends upon a number of factors including the type of test, proportion of men rejected, flight conditions, and preoxygenation, as well as diurnal and seasonal fluctuations in bends susceptibility.

Regarding preselection of divers, high standards of physical fitness are paramount. Welham, Blanch, and Behnke (*2171*) reported in 1944 a procedure of selecting diving and aviation personnel resistant to decompression sickness based on tests in a low-pressure chamber. These and other preselection tests require further validation studies.

2150. Gray, J. S. Symptoms experienced during repeated low-pressure chamber flights, and their significance for high altitude classification. U. S. NRC–CAM. *C. A. M. rept. no. 71,* 1 July 1942, 5 pp. [P]

2151. Gray, J. S. The reliability of procedures for high altitude classification. U. S. NRC–CAM. *C. A. M. rept. no. 98,* 5 November 1942, 4 pp. [P]

2152. Grenell, R., F. D. Humm, L. F. Nims, and H. M. Somberg. The reliability of the decompression subcommittee's 90-minute preselection test. U. S. NRC–CAM. *C. A. M. rept. no. 355,* 5 September 1944, 4 pp.

2153. Henry, F. The reliability of chamber classification for "bends" susceptibility and validity of the inert gas-exchange method. U. S. NRC–CAM. *C. A. M. rept. no. 176,* 2 September 1943, 10 pp. [P]

2154. Henry, F. M. The relation of pain to impairment in motor function in decompression sickness. U. S. NRC–CAM. *C. A. M. rept. no. 397,* 15 December 1944, 6 pp.

2155. Henry, F. M. Altitude pain. A study of individual differences in susceptibility to bends, chokes, and related symptoms. *J. Aviat. Med.,* 1946, *17:* 28–55. [P]

2156. Henry, F. M., S. F. Cook, H. B. Jones, and E. Strajman. Decompression sickness classification tests at 30,000 feet with preoxygenation and exercise, and at 38,000 feet with light exercise. U. S. NRC–CAM. *OEMcmr–196, C. A. M. rept. no. 454,* July 1945, 2 pp. [P]

2157. Henry, F. M., S. F. Cook, J. H. Lawrence, and D. W. Lund. Decompression sickness classification tests with leg exercise and combined arm-leg exercise. U. S. NRC–CAM. *OEMcmr–196, C. A. M. rept. no. 446,* July 1945, 9 pp.

2158. Henry, F. M., S. F. Cook, and D. W. Lund. An effective decompression sickness classification test, and a method for evaluating its usefulness. U. S. NRC–CAM. *C. A. M. rept. no. 421,* 24 February 1945, 14 pp.

2159. Henry, F. M. and A. C. Ivy. Preselection tests. pp. 322–359 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [D]

2160. Henry, F. M., H. B. Jones, J. B. Mohney, and C. A. Tobias. The reliability of decompression chamber classification using the step-up exercise, and the relation of inert-gas exchange and other factors to bends-resistance. U. S. NRC–CAM. *C. A. M. rept. no. 264,* 2 December 1944, 16 pp.

2161. Jones, H. B., C. Tobias, W. F. Loomis, J. B. Mahoney, W. N. Sears, J. C. Larkin, J. G. Hamilton, and J. H. Lawrence. An objective method for the study of the physiology of aeroemphysema and for the selection of high altitude aircrew using the radioactive isotopes of inert gases. U. S. NRC–CAM. *C. A. M. rept. no. 81,* November 1942, 6 pp. [P]

2162. Larrabee, M. G., J. C. Lilly, J. H. Comroe, Jr., and R. Hodes. Decompression sickness during exposures to 38,000 feet, accompanied by exercise. Evaluation of a classification procedure. U. S. NRC–CAM. *C. A. M. rept. no. 137,* 9 June 1943, 20 pp. [P]

2163. Nims, L. F. Decompression sickness selection tests using denitrogenation. Yale Aero-medical research unit, *Rept. no. 43,* 16 April 1945, 2 pp.

2164. Robinson, T. W. High-altitude endurance tests. U. S. NRC–CAM. *C. A. M. rept. no. 205,* 10 August 1943, 5 pp. [P]

2165. Robinson, T. W. High-altitude tolerance tests. U. S. NRC–CAM. *C. A. M. rept. no. 316,* 12 May 1944, 30 pp. [P]

2166. Ryder, H. W., C. D. Stevens, J. P. Webb, and M. A. Blankenhorn. The measurement of decompression sickness. U. S. NRC–CAM. *C. A. M. rept. no. 412,* 15 February 1945, 46 pp. [M]

2167. Savely, H. E. High altitude classification tests. U. S. NRC–CAM. *C. A. M. rept. no. 99,* 31 October 1942, 14 pp. [P]

2168. Stevens, C. D., M. Inatome, H. W. Ryder, E. B. Ferris, and M. A. Blankenhorn. The rate of nitrogen elimination from the lungs and its relation to individual susceptibility to decompression sickness. U. S. NRC–CAM. *OEMcmr–36, C. A. M. rept. no. 456,* July 1945, 19 pp.

2169. U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Materiel command, ENG. Aero medical laboratory. Preselection test for susceptibility to aeroembolism. *ENG–49–095–27,* 30 March 1943, 9 pp. [P]

2170. Walder, D. N. Serum surface tension and its relation to the decompression sickness of aviators. *J. Physiol.,* 1948, *107:* 43P–44P. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 632. Abstr.

2171. Welham, W., J. J. Blanch, and A. R. Behnke. A procedure for selection of diving and aviation personnel resistant to decompression sickness based on tests in a low-pressure chamber. U. S. Navy, Naval gun factory, EDU. *Project X–338 (Av–191–h),* January 1944, 5 pp. [P]

IV. EXPLOSIVE DECOMPRESSION

A. GENERAL STUDIES

This section on explosive decompression has been included because some of the pathological effects of explosive decompression are similar to those pulmonary lesions found in escape accidents. Also, air embolism occurs in explosive decompression to high altitudes as in decompression sickness caused by too rapid ascent from pressures greater than 1 atmosphere. In explosive decompression, there is generally a short initial rise of arterial blood pressure followed by a prolonged slowing of the heart and fall of arterial blood pressure in part due to decompression

effects and in part due to anoxia. There is a brief rise in cerebrospinal fluid pressure, paralleling the rise in intrathoracic pressure. Following the period of explosive decompression there is apnea. Temperature within the lungs drops due to evaporation of moisture and to gas expansion. There is an increase in the alveolar carbon dioxide and oxygen. In some cases there are hemorrhages and liver-like consolidation of the lungs. Pulmonary blood flow is impeded. Intravascular bubbles are observed in animals explosively decompressed to 30 mm. Hg. Anoxic anoxia and air embolism are considered the major lethal factors in explosive decompression injury. Intrapulmonary gas expansion, while a cause of lung lesions, is not considered so important as a lethal agent.

For general studies on explosive decompression, the references given below should be consulted.

2172. Clamann, H. G. Explosive decompression tests on human subjects. 1. Interim report: tests of explosive decompression without oxygen. U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. S2–46–9,* (Translated German document), 25 March 1946, 6 pp. [P]

2173. Comfort, E. Anoxia following explosive decompression from altitudes below 10,000 feet. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. MCREXD–696–111A,* 10 May 1948, 10 pp. [P]

2174. Fulton, J. F. Altitude sickness and acclimatization. The history of oxygen. pp. 3–48 in: *Aviation medicine in its preventive aspects. An historical survey.* London, Oxford University Press, 1948, 174 pp. [R]

2175. Gelfan, S. Explosive decompression of monkeys to extreme altitudes (motion picture). *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 47.

2176. Haber, F. Physical process of explosive decompression. *J. Aviat. Med.,* 1950, *21:* 495–499. USAF. School of aviation medicine, Randolph Field, Tex. Department of space medicine, *Special Rept.,* October 1950, 7 pp.

2177. Millet, P. Décompression explosive au cours d'une montée a 40.000 pieds. *Méd. aeronaut.,* 1950, *5:* 151–153. [D]

2178. Wilson, J. W. Explosive decompression at high altitude. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. TSEAA–696–104B,* 11 August 1947, 21 pp. [P]

2179. Wilson, J. W. Explosive decompression to 30 mm. Hg. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. MCREXD–696–104I,* 18 June 1948, 76 pp. [P]

B. EFFECTS OF EXPLOSIVE DECOMPRESSION ON HEART AND CIRCULATION

Experimental animals explosively decompressed show a drop in systemic arterial blood pressure and bradycardia. Whitehorn, Lein, and Edelmann (*2189*) 1945 decompressed anesthetized dogs at rates greater than 20 lbs. per sq. in. per second over a range of 435 mm. Hg. The extent of the blood-pressure fall in these animals was found to vary directly with the rate and range of the decompression. Increasing the resistance to respiration markedly increased the severity of blood-pressure drops at a given rate and range of decompression. Increased intrathoracic pressure with distention of the lungs, occurring when the rate of decompression of the chamber exceeded the rate at which the lungs could decompress, was considered to be the primary cause of the fall in arterial pressure. Reflexes from distended abdominal organs were believed to play a contributing part. Livingston (*2187*) 1951 and Gelfan and Werner (*2184* and *2185*) 1951 have given reports on blood-pressure changes following explosive decompression of monkeys to extreme altitudes. Monkeys can withstand the stress of sudden decompression to altitudes as high as 75,000 feet simulated altitude provided that they are recompressed at free-fall rates in 100 percent oxygen. At the moment of decompression there is a brief reflex cardiac slowing that is a function of the decompression rate but independent of anoxia (*2182* and *2187*). This initial slowing is probably mediated by the vagus nerve and appears to be initiated by pressor receptors responding to the mechanical effects of decompression. After a latent period of about 40 seconds, a prolonged bradycardia supervenes caused by the effects of complete anoxia on the central nervous system with some direct influences on the heart itself. Negative middle-ear pressure may initiate reflex bradycardia occurring in the unanesthetized animals during recompression at a free-fall rate. Reversible blood-pressure changes following sudden decompression to very high altitudes are due to mechanical factors and the very rapidly induced total anoxia (*2184* and *2185*). The extremely rapid rate of ambient pressure change has an initial Valsalva-like effect and causes an instantaneous blood-pressure rise. This sudden rise of blood pressure elicits from the carotid sinus and the aortic arch an immediate, but brief, reflex cardiac slowing and slight lowering of blood pressure. The vagal discharge is usually intense enough to produce sinus arrest for a period of 1 to 4 cardiac cycles. The entire duration of this decompression response is less than 10 seconds. Following decompression to altitudes at which a positive intra-abdominal pressure inevitably develops, the resulting interference with venous return from the lower part of the body causes an additional lowering of the arterial blood pressure. Within 20 seconds, the blood pressure may drop precipitously to 50 percent of the predecompression level. This precipitous drop is due also to the rapidly induced total anoxia at

altitudes above 52,000 feet, even in 100 percent oxygen. Although the rate of establishing total anoxia is explosive, the latent period for the beginning of the anoxic fall in arterial blood pressure is about 20 seconds. The mechanical effects thus precede the anoxic ones. This circulatory impairment probably hastens the establishment of tissue anoxia. The evidence suggests that the rapidly induced total anoxia and simultaneous acapnia quickly render the vasomotor center unresponsive to chemoreceptor influence. Recovery is prompt if the animal chamber is recompressed within the latent period for the anoxic cardiovascular effects. With free-fall descent rates in oxygen, blood-pressure recovery to within 10 percent of control levels is a function of the time interval to reach altitudes. Intra-abdominal pressure equalization occurs during free-fall when the monkeys are still at completely anoxic altitudes during free-fall descent. The mechanical interference with adequate diastolic filling of the heart is thus first to be eliminated during descent just as this factor is the first to influence the blood pressure immediately after decompression. Contrary to previous reports, Gelfan and Werner (*2184*) 1951 stated that the pulse pressure throughout the period beginning immediately upon decompression never disappears, even at final ambient pressures of 20 to 26 mm. Hg.

Cardiac changes following explosive decompression to simulated altitudes as high as 75,000 feet were studied in anesthetized monkeys by Dowling and Gelfan (*2181*) 1949 by means of unipolar lead electrocardiography, recording simultaneously from three extremity leads. The first observable change in the electrocardiogram complex is displacement of the S–T segment, which occurs between 5 to 30 seconds after the sudden decompression. This change is quickly followed by an increase in the P–R interval and simultaneously an absolute shortening of the Q–T interval, even during the marked bradycardia that develops. The Q–T interval shortening indicates an acceleration of repolarization, and there are indications that it is the left anterior ventricle that repolarizes faster than the rest of the heart. The increase in irritability of this part of the heart is indicated not only by electrocardiographic changes but also by the extrasystoles that arise from the left anterior ventricle. Heart block ranging from first degree to complete block is also observed. The electrocardiographic complex returns to normal after recompression to sea level. These cardiac changes are believed by the authors to be due to anoxia rather than pressure changes since the same alterations have been observed in nitrogen anoxia without pressure changes. Also, sudden decompression from sea level to 40,000 feet simulated altitude in oxygen, at which altitude the anoxia is insignificant, does not alter the electrocardiographic complex. Electrocardiographic changes following explosive decompression of dogs to 30 mm. Hg have been reported by Burch (*2180*) 1949. In a previous communication, this author had reported that dogs explosively decompressed to a terminal pressure of 30 mm. Hg died of venticular fibrillation, which developed about 80 seconds after the explosion. This conclusion was derived from direct observation on the heart through a plastic window sutured to the anterior chest wall. The radical surgery involved may have been a factor in producing the fibrillation, and to test this possibility the author explosively decompressed a series of intact, anesthetized dogs recording the electrocardiograms continuously. About 60 seconds after the explosion, changes in rhythm were noted. There was auriculoventricular block, interventricular block, and idioventricular rhythms but no evidence of ventricular fibrillation. About 2 minutes after the explosion a severe slowing of the heart occurred. This was considered significant since previous chest-window observations showed that cessation of the heart occurred within 2 seconds after such explosions. The author concluded that the surgical procedure tended to precipitate ventricular fibrillation.

For further studies on the cardiovascular effects of explosive decompression, papers by Hitchcock, Beman, and Kemph (*2186*) 1948 and Vail and Hitchcock (*2188*) 1949 should be consulted.

2180. Burch, B. H. Electrocardiographic observations following explosive decompression of dogs to 30 mm. Hg. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 19.

2181. Dowling, R. and S. Gelfan. Cardiac changes in monkeys following explosive decompression to extreme altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 36–37.

2182. Gelfan, S. Explosive decompression of Macaque monkeys to extreme altitudes and recompression at free-fall rates. *J. appl. Physiol.*, 1950, *3:* 254–281. [P]

2183. Gelfan, S. and G. D. Davis. Explosive decompression of monkeys at extreme altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 41.

2184. Gelfan, S. and A. Y. Werner. Blood pressure changes following explosive decompression of monkeys to extreme altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 48.

2185. Gelfan, S. and A. Y. Werner. Cardiovascular responses following explosive decompression of Macaque monkeys to extreme altitudes. *J. appl. Physiol.*, 1951, *4:* 280–310.

2188. Vail, E. G. and F. A. Hitchcock. Effects of explo-Estimation of subcutaneous pressure in animals explosively decompressed to pressures of 30 mm. Hg. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 55. [P]

2187. Livingston, R. B. Addendum. pp. 396–397 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for

the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp.

2188. Vail, E. G. and F. A. Hitchcock. Effects of explosive decompression on blood temperature in the right and left heart. *Fed. Proc. Amer. Soc. exp. Biol.,* 1949, *8:* 168.

2189. Whitehorn, W. V., A. Lein, and A. Edelmann. The effect of explosive decompression on the blood pressure of anesthetized dogs. U. S. NRC–CAM. *OEMcmr–74. C. A. M. rept. no. 479,* 13 September 1945, 9 pp.

C. EFFECT OF EXPLOSIVE DECOMPRESSION ON CEREBROSPINAL FLUID PRESSURE

The effect of both slow and explosive decompression upon cerebrospinal fluid pressure of anesthetized dogs was measured by Whitehorn, Lein, Edelmann, and Hitchcock (*2190*) 1947 by means of a closed optical manometer system. The cerebrospinal fluid pressure was recorded from a needle inserted in the cisterna magna. Decompression to 141 mm. Hg in about 10 minutes resulted in an average rise of 3.0 mm. Hg cerebrospinal fluid pressure which persisted as long as the reduced pressure was maintained. Explosive decompression from a pressure of 522 mm. Hg to 141 mm. Hg in 0.01 or 0.08 second resulted in cerebrospinal fluid pressure rises of 22.5 mm. Hg and 11.6 mm. Hg, respectively, and persisting for only 1.5 seconds. No bubbles were observed. The rise in cerebrospinal fluid pressure was considered by the authors to be a reflection of a similar rise in intrathoracic pressure. The brief duration of the rise in cerebrospinal fluid pressure and its relationship to the rate of decompression indicated to the authors that the causal factor is the change in intrathoracic pressure rather than the increased abdominal pressure.

2190. Whitehorn, W. V., A. Lein, A. Edelmann, and F. A. Hitchcock. The effect of explosive decompression on cerebrospinal fluid pressue. *Amer. J. Physiol.,* 1947, *148:* 253–258. [P]

D. EFFECTS OF EXPLOSIVE DECOMPRESSION ON THE RESPIRATORY SYSTEM

Hitchcock and Edelmann (*2196*) 1947 explosively decompressed a series of dogs to 30 mm. Hg and kept them at this pressure for 15 to 120 seconds. The sequence of events following explosion was as follows: first, the respiration became deep and rapid, then abdominal distention occurred and the animals collapsed, and there were mild convulsions. The animals then became quiescent except for occasional gasping movements. Lacrimation, salivation, and urination occurred. All visible respiratory movements ceased about 30 seconds after the explosive decompression. Shortly after this, subcutaneous swelling started in the lower abdomen and progressed headward. Thirty to 35 seconds after the explosion the eyes were glazed and the animals appeared to be dead, and remained in this condition until recompression. When the animals were recompressed to about 55 mm. Hg the distention of the body decreased, and at 100 mm. Hg the dogs were almost back to normal size. When normal barometric pressure was reached and the chamber was opened, the animals had invariably ceased breathing but the heart was still beating. Respiration reappeared within 30 seconds after return to atmospheric pressure. The corneal reflexes returned 3 to 7 minutes later. Several dogs kept at terminal pressure for 1 minute or longer showed decerebrate rigidity. This developed about 6 minutes after the explosion and lasted for about 3 minutes. The dogs were usually on their feet 12 to 13 minutes after the explosion, and 20 minutes after return to normal barometric pressure, the animals were behaving without symptoms or signs. The authors considered that all of the effects except the swelling of the body are due to acute anoxia.

The volume and composition of air expelled from the lungs during explosive decompression has been studied by Hitchcock, Edelmann, Shelden, and Whitehorn (*2197*) 1946. The effect of explosive decompression upon the temperature of the lungs in anesthetized dogs has been investigated by Vail and Hitchcock (*2200*) 1948. A thermistor located in the trachea recorded the temperature of the inspired and expired air. The temperature of expired air never reached the temperature recorded in the deep lung. Measurements of the temperature at various levels in the pulmonary tract wave a mean temperature in the trachea of 34.5° C., and in the deep lung of 37.1° C. At explosive decompression, tank temperatures were found to decrease an average of 2.0 C. for all terminal pressures. The greatest drop occurred in 0.2 second. Respiratory patterns showed many variations. The point in a respiratory cycle at which the explosion occurred had a pronounced effect upon the respiratory pattern. The tracheal temperature fell during decompression and remained at a low level until recompression. The average decrease in tracheal temperature was 8.8° C. Although attempted respiratory movements were observed in these animals, no ventilation of the lungs occurred. The temperature drop in the lungs occurred in two phases. The first phase was considered to be due probably to the expanding lung gases and the second to the vaporization of water.

Regarding the relationship between the phases of respiration and the amount of lung damage produced by explosive decompression, Berg, Baumberger, Crescitelli, Rapaport, and Greeley (*2191*) 1943 carried out experimental studies on the rat.

The respiration of individual rats was photographically recorded, using a string galvanometer in conjunction with sensitive thermocouples which gave electrical variations due to the difference in temperature between inspired and expired air. Explosive decompression produced a sudden deflection of the string which was caused by the rapid expiration of expanded air from the lungs. This served accurately to place the time of decompression in the respiratory cycle. All rats were explosively decompressed from ground level to 40,000 feet simulated altitude in approximately 0.02 second. They were breathing 100 percent oxygen and were returned to the ground level in about 30 seconds. Lung damage occurred throughout inspiration and during the first one-third of expiration. Slight or no damage was found during the last two-thirds of expiration. A period of apnea always followed the decompression.

Alveolar gases were analyzed by Luft, Clamann, and Adler (*2198*) 1951 in subjects before and immediately after rapid decompression to various equivalent altitudes up to 52,000 feet. Alveolar oxygen as well as carbon dioxide percentages increased immediately after decompression when air was breathed. The higher the equivalent altitude reached, the greater was the increase in alveolar oxygen and carbon dioxide. At 50,000 feet the alveolar oxygen reached a value of 27 percent and the carbon dioxide 40 percent. When oxygen was breathed during the decompression, alveolar oxygen was reduced at the expense of carbon dioxide, the latter reaching a value of 56 percent after decompression to 52,000 feet simulated altitude. These results are explained by the authors by the fact that the normal carbon dioxide and oxygen tensions are suddenly reduced below the level existing in the pulmonary blood. Thus both of these gases pass from the blood to the alveoli and crowd out the nitrogen when air is breathed. When oxygen is breathed, only carbon dioxide, oxygen, and water vapor compete for the alveolar space.

In an experimental study of the effects of explosive decompression, Corey (*2193*) 1947 carried out 300 tests on rats and cats explosively decompressed to an altitude equivalent of 80,000 feet. Recompression was carried out usually at a rate to simulate that of a freely falling man until the level of 18,000 feet was reached. Thereafter, a rate of fall of 20 feet per second, simulating a parachute descent, was maintained. No fatal injuries were observed in explosive decompressions below 35,000 feet. From this level up to 80,000 feet, slightly more than 50 percent of the animals succumbed. Even at the latter level, however, a few animals survived following very rapid recompression. The injuries produced were limited to the lungs and gastro-intestinal tract. Pulmonary hemorrhage and bleeding into the gastrointestinal tract with occasional perforations were observed. In cases of fatal decompression, the heart rate fell progressively and the rhythm became irregular. The severity of the injury from explosive decompression would appear, according to the author, to depend upon the volume of gas within the lungs (that is to say, the phase of respiration) and the gastrointestinal tract at the moment of decompression. The severity of the injury also depends upon the length of time the animal is maintained at the simulated high altitude. It was observed that in all cases in which the expansion of the lungs was restricted by a simple strap around the upper part of the body, no fatality occurred from explosive decompression. Also in tests in which very rapid (instantaneous) recompression was made, a much larger number of animals survived. Multiple explosive decompressions carried out on dogs were found to increase the extent of pulmonary hemorrhage in comparison with animals decompressed only one time (Burkhardt, Coulson, Criscuolo, and Adler (*2192*) 1951).

Pathological changes in rats explosively decompressed to high altitudes have been examined by Wilson (*2201*) 1947. In Wilson's studies more than 200 rats were explosively decompressed in a chamber from a simulated altitude of 20,000 feet up to altitudes ranging to a maximum of 75,000 feet. Grossly visible, intravascular bubbles were infrequently found and when they did occur, tended to be seen most often in the veins of rats decompressed to above 50,000 feet. Hemorrhages into the cochlea occurred in more than one-third of the animals decompressed to above 45,000 feet. Rats dying at altitudes above 50,000 feet tended to show liverlike consolidation of the lungs. In these rats there was nearly complete obstruction to blood flow through the pulmonary bed.

For further studies on the effects of explosive decompression upon the lungs, papers by the following may be consulted: Hall (*2194*) 1950; Hall and Hall (*2195*) 1951; and USAF, Wright-Patterson Air Force Base, Dayton, Ohio, Aero Medical Laboratory (*2199*) 1949.

2191. Berg, W. E., J. P. Baumberger, F. Crescitelli, S. Rapaport, and P. O. Greeley. Explosive decompression: lung damage correlated with the respiratory cycles in explosive decompression. U. S. NRC–CAM. *C. A. M. rept. no. 173,* 16 August 1943, 7 pp. [P]

2192. Burkhardt, W. L., C. K. Coulson, D. Criscuolo, and H. F. Adler. Explosive decompression. II. The mechanical effect of multiple explosive decompressions.

USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–23–005, rept. no. 2,* August 1951, 8 pp.

2193. Corey, E. L. Tests on explosive decompression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 91.

2194. Hall, F. G. Pattern of gas expulsion from human lungs during rapid decompression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 55. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Technical rept. no. 6239,* September 1950, 16 pp.

2195. Hall, F. G. and K. D. Hall. Expulsion of respiratory gases from lungs of human subjects during rapid decompression. *J. appl. Physiol.,* 1951, *4:* 1–6.

2196. Hitchcock, F. A. and A. Edelmann. The response of normal dogs to explosive decompression to 30 mm. of Hg. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 130.

2197. Hitchcock, F. A., A. Edelmann, F. F. Shelden, and W. V. Whitehorn. The volume and composition of air expelled from the lungs during explosive decompression. *Fed. Proc. Amer. Soc. exp. Biol.,* 1946, *5:* 48.

2198. Luft, U. C., H. G. Clamann, and H. F. Adler. Alveolar gases in rapid decompression to high altitudes. *J. appl. Physiol.,* 1949, *2:* 37–48. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 300. Abstr.

2199. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. Aero medical laboratory, ENG. Explosive decompression, pp. 11–13 in: *Synopsis of the aero medical aspects of jet propelled aircraft.* January 1949, 46 pp. [R]

2200. Vail, E. G. and F. A. Hitchcock. Effect of explosive decompression on the temperature of the lungs. *Amer. J. Physiol.,* 1948, *155:* 473–474. Abstr.

2201. Wilson, J. W. Pathology in rats explosively decompressed to high altitudes. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. Aero medical laboratory. *Technical rept. TSEAA–696–104C,* 12 August 1947, 17 pp. [P]

E. EFFECT OF EXPLOSIVE DECOMPRESSION ON OCCURRENCE OF INTRAVASCULAR BUBBLES

Whitehorn, Lein, and Hitchcock (*2203*) 1947 subjected animals to explosive decompression and subsequent brief periods of exposure to reduced barometric pressures. Of 13 guinea pigs dying during such exposures, 7 showed intravascular gas bubbles after recompression. No bubbles were found in animals surviving the exposure. In dogs subjected to explosive decompression, Kemph and Hitchcock (*2202*) 1948 found no intravascular bubbles 30 seconds after explosive decompression to barometric pressures greater than 55 mm. Hg. Bubbles were a frequent finding within 30 seconds at lower barometric pressures and a constant finding after 1 minute exposure to 30 mm. Hg. Bubbles were observed in superficial arteries within 30 seconds, and in veins within 3 minutes after explosive decompression to 30 mm. Hg. The authors concluded that intravascular bubbles were formed centrally rather than peripherally; that is to say, in the large veins, heart, or pulmonary system. The circulation was probably blocked by these bubbles. Determinations of blood gases showed considerable oxygen present after explosive decompression to pressures less than 50 mm. Hg. Therefore, stagnation anoxia and other factors, rather than anoxic anoxia, were considered significant in the etiology of the effects of rapid decompression to barometric pressures below the vapor pressure of body fluids. Whitehorn, Lein, and Hitchcock (*2203*) considered that intravascular bubble formation was a negligible hazard in explosive decompression. It was observed that the outstanding feature associated with death was abdominal distention. It seemed likely to the authors that anoxia, probably intensified by interfercnce with respiratory movements as the result of abdominal distention, was the prime cause of fatalities.

2202. Kemph, J. P. and F. A. Hitchcock. Changes in the blood following explosive decompression. *Amer. J. Physiol.,* 1948, *155:* 477. Abstr.

2203. Whitehorn, W. V., A. Lein, and F. A. Hitchcock. The effect of explosive decompression on the occurrence of intravascular bubbles. *J. Aviat. Med.,* 1947, *18:* 392–394. [P]

F. LETHAL FACTORS IN EXPLOSIVE DECOMPRESSION INJURY

In explosively decompressed rats and cats, Corey (*2204*) 1947 observed pulmonary hemorrhage in all animals exposed to pressure equivalents of 50,-000 feet and 80,000 feet. No pulmonary lesions were found in animals decompressed to simulated altitudes below 35,000 feet. The left lung showed less extensive trauma than did the right. In both lungs the apical poles, the posterior surfaces, and the thin, pulmonary margins appeared to be the most vulnerable areas. Hall and Corey (*2213*) 1950 considered that anoxic anoxia was of major importance as a causative factor in death resulting from explosive decompression injury in animals decompressed to an altitude equivalent of 80,000 feet. According to Corey and Lewis (*2207*) 1950, the duration of post-decompression anoxia represents the major factor in determining the outcome of cxplosive decompression. Injection of atropine or mecholyl significantly reduced the mortality in rats exposed to a standardized decompression invariably lethal to untreated animals. Anesthesia with ether, evipal, or pentothal permitted all rats tested to survive explosive decompression which was uniformly fatal to control animals.

Corey (*2205* and *2206*) 1949 explosively decompressed rats to normal atmospheric pressure after exposure to positive pressures of 2 to 20 atmospheres for varying intervals of time. Decompression from 2 to as much as 6 atmospheres (equivalent to a gas-expansion differential of 18,000 to 42,000 feet) was well tolerated and such decompressions may be con-

sidered to be entirely innocuous in the rat. Of rats decompressed after 30 minutes' exposures to 7 to 11 atmospheres, 77 percent died. Air embolism was present in 82 percent of these animals, with pulmonary lesions in 18 percent of all cases. All animals succumbed following decompression from 11 atmospheres (a gas-expansion equivalent of 55,000 feet) when so maintained for 30 minutes prior to release of pressure. Without exception these animals exhibited gas emboli, while pulmonary hemorrhages were seen in only 15 percent. All rats dying following explosive decompression from 20 atmospheres gave evidence of severe aeroembolism, while pulmonary lesions could be demonstrated in only 43 percent of such animals. Decompression after a 50-second exposure to 30 atmospheres was invariably fatal. On the other hand, all animals survived this pressure change when the time under pressure was reduced to 10 seconds. These experiments indicated to the author that anoxic anoxia and aeroembolism constitute the major factors in the etiology of explosive decompression injury, and that intrapulmonary gas expansion may be considered of relatively minor importance as a lethal agent.

In considering the pathological lesions caused by explosive decompression, Edelmann, Whitehorn, Lein, and Hitchcock (*2208*) 1946 believed sudden increases in intrapulmonary pressure produced by explosive decompression to be the primary etiological agent in producing lesions in dogs explosively decompressed and rapidly recompressed to avoid anoxia as a complicating factor. Fusco, Mellette, and Hitchcock (*2210*) 1948 found that edema and hemorrhage of the lungs could be produced in rats exposed to nitrogen, but these lung lesions were not as great as in rats explosively decompressed to 30 mm. Hg. Therefore, it was considered that only a part of the effects of explosive decompression on the lungs are due to anoxia. Whitehorn, Lein, and Hitchcock (*2217*) 1947 reported that binding the abdomen and lower thorax of dogs did not protect against the occurrence of pulmonary hemorrhages. They stated that binding seems to increase the tendency to pathological lesions through the bruising action of the lungs against rigid thoracic walls.

For further studies on lethal factors in explosive decompression injury, papers by the following may be consulted: Fulton (*2209*) 1941; Gelfan, Nims, and Livingston (*2211*) 1947; Gressly and Meakin (*2212*) 1943; Kemph and Hitchcock (*2214*) 1951; Mahoney (*2215*) 1949; and Smith (*2216*) 1946.

2204. Corey, E. L. An experimental study of explosive decompression injury. *Amer. J. Physiol.*, 1947, *150:* 607–612. *J. industr. Hyg.*, 1948, *30:* abstract section: 85–86. [P]

2205. Corey, E. L. Factors in explosive decompression injury. *Amer. J. Physiol.*, 1949, *157:* 88–93. [P]

2206. Corey, E. L. Conditions influencing explosive decompression injury. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 29. [P]

2207. Corey, E. L. and E. G. Lewis. Etiology of explosive decompression injury. *Amer. J. Physiol.*, 1950, *162:* 452–457. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 25.

2208. Edelmann, A., W. V. Whitehorn, A. Lein, and F. A. Hitchcock. Pathological lesions produced by explosive decompression. *J. Aviat. Med.*, 1946, *17:* 596–601. [P]

2209. Fulton, J. F. Explosive decompression and pressure cabin aircraft. U. S. NRC–CAM. *C. A. M. rept. no. 33,* 11 November 1941, 4 pp.

2210. Fusco, M., H. Mellette, and F. A. Hitchcock. Determination of the etiology of pathological effects of explosive decompression on the lungs of rats. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 39. [P]

2211. Gelfan, S., L. F. Nims, and R. B. Livingston. Cause of death from explosive decompression at high altitudes. *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 110.

2212. Gressly, D. W. and L. W. Meakin. Explosive decompression—effects on human subjects. U. S. NRC–CAM. *C. A. M. rept. no. 220,* 24 April 1943, 4 pp. [P]

2213. Hall, W. M. and E. L. Corey. Anoxia in explosive decompression injury. *Amer. J. Physiol.*, 1950, *160:* 361–365. *Abstr. World Med.*, 1950, *8:* 456. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1211. [P]

2214. Kemph, J. P. and F. A. Hitchcock. X-ray studies of effects of high intrapulmonic pressures on heart, lungs and thoracic cage of dogs at 30 mm. Hg ambient pressure. *Amer. J. Physiol.*, 1951, *167:* 801–802. Abstr.

2215. Mahoney, D. I. Repeated explosive decompression. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 104. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Memo. Rept. MCREXD–696–107H,* 15 December 1948, 3 pp.

2216. Smith, J. J. The physiological and pathological effects of explosive decompression. *Northwestern University, Summaries of doctoral dissertations.* 1946, *15:* 215–217.

2217. Whitehorn, W. V., A. Lein, and F. A. Hitchcock. The effect of binding of the abdomen and thorax on pulmonary lesions produced by explosive decompression. *J. Aviat. Med.*, 1947, *18:* 102–104. [P]

G. TOLERANCE OF EXPLOSIVE DECOMPRESSION

Experiments of Hitchcock (*2223*) 1951 have led him to conclude that explosive decompression at rates and over ranges likely to occur with modern aircraft is not a serious hazard. For other studies of tolerance of explosive decompression, references listed below should be consulted.

2218. Allen, S. C. Ability of human subjects to withstand "explosive decompression." *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 68. [P]

2218a. Burkhardt, W. L., R. E. Hedblom, A. W. Hetherington, and H. F. Alder. Extent of pathological damage to animals explosively decompressed in a cold environment. *J. Aviat. Med.*, 1950, *21:* 304–308; 320.

2219. Gagge, A. P., and R. S. Shaw. Explosive decompression. pp. 49–50 in: *Medical physics. Volume II.*

Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

2220. Gelfan, S., L. F. Nims, and R. B. Livingston. Explosive decompression at high altitude. *Amer. J. Physiol.*, 1950, *162:* 37–53. [P]

2221. Hall, W. M. and E. L. Corey. Anoxia in explosive decompression injury. *Amer. J. Physiol.*, 1950, *160:* 361–365.

2222. Hiestand, W. A. and F. W. Stemler. Rapidly acquired tolerance to decompression in insects. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 63–64.

2223. Hitchcock, F. A. Explosive decompression. pp. 378–395 in: *Decompression sickness. Caisson sickness, diver's and flier's bends and related syndromes.* Edited by J. F. Fulton for the Subcommittee on decompression sickness, National Research Council. Philadelphia, W. B. Saunders Co., 1951, 437 pp. [D] [P]

2224. Hitchcock, F. A., W. V. Whitehorn, and A. Edelman. Tolerance of normal men to explosive decompression. *J. appl. Physiol.*, 1948, *1:* 418–429. [P]

2225. Pivovarov, M. A. and G. L. Komendantov. O trenirovke organizma k rezkim perepadam barometrichesogo davleniia. [Training of the organism to sharp falls in barometric pressure.] pp. 252–266 in: *Trudy Voenno-Meditsinskoi Akademii Im. Kirova,* edited by: L. A. Orbeli, N. N. Anichkova, I. P. Petrova, A. V. Lebedinskogo. Moskva, 1946, 269 pp.

2226. Rockhold, W. T., F. W. Stemler, J. E. Wiebers, and W. A. Hiestand. Survival time of the mouse as related to ambient pO_2 produced by explosive decompression. *Proc. Soc. exp. Biol., N. Y.*, 1950, *73:* 331–332. [P]

V. OXYGEN INTOXICATION

A. EFFECTS OF INCREASED OXYGEN TENSION NOT IN EXCESS OF ONE ATMOSPHERE

1. GENERAL STUDIES

For a comprehensive review of the literature on oxygen intoxication, the reader should consult the section on this subject (pp. 163–194) in the first volume of this Sourcebook. Reference should be made to the classical studies of Paul Bert cited in the first volume of the Sourcebook and to the work of Bean also cited there. The toxic effects of an excess of oxygen have always been and still remain a subject of interest and importance. The mechanisms of these toxic effects are still not entirely clear. Observations and investigations of the past have distinguished two principal manifestations of oxygen poisoning. The first is the so-called Lorrain Smith effect or subacute poisoning, which consists of an irritation of the pulmonary alveoli and develops as a result of exposure to oxygen tensions of about 0.7 to 0.8 atmosphere of oxygen. The second manifestation is the so-called Paul Bert effect and consists of generalized epileptiform convulsions produced by prolonged inhalation of oxygen at pressures greater than 1 atmosphere. Although the pulmonary manifestations are characteristically observed at relatively lower oxygen tensions, while the convulsive effects are characteristic of high oxygen tensions, nevertheless, the lungs may also be involved at very high pressures of oxygen.

Exposure to oxygen in concentrations above 60 percent of 1 atmosphere for sufficient lengths of time produces toxic effects on both animals and human beings. The severity of these effects is proportional to the concentration and to the duration of exposure and varies from individual to individual as well as from one species to another (*2235*). Under these conditions, oxygen acts adversely upon the lungs, the blood, and other tissues of the body, including to some extent the central nervous system. Symptoms in human subjects include substernal distress, nasal congestion or coryza, conjunctival irritation, significant decrease in vital capacity, discomfort in the ears, and fatigue. Schmidt and Brooks (*2234*) 1949 elicited respiratory symptoms in 90 healthy, young men between the ages of 19 and 31 years who were exposed to oxygen for 24 hours at 1 atmosphere. Substernal distress was produced in 82 percent of the subjects and there was a significant decrease in vital capacity. Signs of nose and throat irritation were common. Intermittence of oxygen supply produced by 15 minutes breathing of normal air every 3 hours did not decrease the incidence of complaints. In anesthetized cats and dogs breathing pure oxygen at normal barometic pressure, Beznak and Liljestrand (*2228*) 1949 found a reduction of lymph flow from the right thoracic duct amounting to about 30 percent. Intestinal movements showed an increase. The authors considered that oxygen inhalation under the condition of their experiments produced alteration of the permeability of the capillaries or the colloid osmotic pressure or both. With regard to the lungs, a blocking effect of the dilated precapillaries upon the lymphatic seemed possible.

In studies carried out by Comroe, Dripps, Dumke, and Deming (*2231*) 1945, the administration of 100 percent oxygen to a large group of healthy men continuously for 24 hours at normal barometric pressure produced substernal distress in 86 percent of the subjects. Breathing 75 percent oxygen produced symptoms in only 55 percent of the subjects, and breathing 50 percent oxygen led to no symptoms. Breathing 100 percent oxygen at a simulated high altitude of 18,000 feet did not produce symptoms, suggesting that the symptoms are due to high oxygen tension and not to elimination of nitrogen. The authors believed that the administration of 100 percent oxygen for short periods up to 12 hours is probably completely safe, but when oxygen must be given in excess of 12 hours it should be reduced to 60 percent unless this is insufficient to saturate the arterial blood. If 100 percent oxygen must be

administered, a careful check should be made of the symptoms most likely to occur as result of high tensions of oxygen.

For other general studies on the effects of increased oxygen tension not in excess of 1 atmosphere, papers by the following may be consulted: Baetjer (*2227*) 1951, Binet and Bochet (*2229*) 1951, Comroe and Dripps (*2230*) 1950, Cotten and Walton (*2232*) 1951, and Patel (*2233*) 1946.

2227. **Baetjer, A. M.** The effects of high and low barometric pressures. pp. 996–1004 in: *Rosenau preventive medicine and hygiene.* Edited by Kenneth F. Maxcy. Seventh edition. New York, Appleton-Century-Crofts, Inc., 1951, 1462 pp.

2228. **Beznak, A. B. L. and G. Liljestrand.** The effect of variations in oxygen tension on the lymph flow. *Acta physiol. scand.,* 1949, *19:* 170–186. [P]

2229. **Binet, L. and ( ) Bochet.** Le séjour prolongé dans l'oxygène pur. *Biol. méd., Paris,* 1951, *40:* 85–95. [R]

2230. **Comroe, J. H. and R. D. Dripps.** Inhalation of oxygen by normal man. pp. 3–18 in: *The physiological basis for oxygen therapy.* Springfield, Charles C. Thomas, 1950, 85 pp. [D]

2231. **Comroe, J. H., Jr., R. D. Dripps, P. R. Dumke, and M. Deming.** The effect of inhalation of high concentrations of oxygen for 24 hours upon normal men at sea level and at a simulated altitude of 18,000 feet. U. S. NRC–CAM. *OEMcmr–28, C. A. M. rept. no. 414,* 5 March 1945, 1 p.

2232. **Cotten, M. de V. and R. P. Walton.** The effects of high oxygen atmospheres on drug induced convulsions. *Anesthesiol.,* 1951, *12:* 491–499.

2233. **Patel, J. C.** Toxicity of oxygen. *Indian Physician,* 1946, *5:* 242–246.

2234. **Schmidt, C. F. and J. W. Brooks.** Oxygen. 5 pp. from: Basic Science Notes. U. S. Army. Medical department, Research and graduate school. Volume No. 6, 1949, Department of Army, Washington, D. C. [P]

2235. **Snapp, F. E., and H. F. Adler.** Oxygen toxicity. USAF. Randolph Field, Tex. School of aviation medicine. *Project Rept. 9,* November 1948, 4 pp. [R]

2. EFFECTS ON THE CENTRAL NERVOUS SYSTEM

Although the effects of oxygen-air mixtures or pure oxygen at normal barometric pressure are predominantly upon the respiratory, circulatory, and metabolic functions, nevertheless, some effects upon the central nervous system have been elucidated. Of particular interest in connection with the central nervous system effects of oxygen at normal barometric pressure is the so-called parodoxical oxygen effect which is often observed on administration of oxygen under conditions of preexisting hypoxia. For a consideration of the oxygen paradox, the appropriate section in this Sourcebook may be consulted (p. 197).

Beyne, Chauchard, and Chauchard (*2236*) 1946 found in guinea pigs that respiration of a hyperoxygenated atmosphere produces a lengthening of chronaxie of motor nerves. In 42 students breathing pure oxygen at normal atmospheric pressure, Binet, Strumza, and Levy (*2237*) 1951 found an increase in the number of errors in intellectual performance tests as compared to performance when breathing ordinary air.

2236. **Beyne, J., B. Chauchard, and P. Chauchard.** Effects de la respiration en atmosphère suroxygénée sur l'excitabilité nerveuse de l'homme. *C. R. Soc. Biol., Paris,* 1946, *140:* 411–412. [R]

2237. **Binet, L., M. V. Strumza, and J. Levy.** Effects de l'inhalation d'oxygène pur, à la pression atmosphérique, sur les facultés intellectuelles de l'homme normal. *C. R. Acad. Sci., Paris,* 1951, *232:* 1527–1529. [P]

3. EFFECTS ON THE CARDIOVASCULAR SYSTEM

The evidence of the literature is in general agreement that respiration of oxygen or hyperoxygenated air at normal atmospheric pressure results in a slowing of the heart. Cardiac slowing occurred in most of the subjects who inhaled 100 percent oxygen in experiments carried out by Dripps and Comroe (*2240*) 1947. In these subjects there was an immediate decrease in pulse rate and respiratory minute volume. This suggested to the authors that some chemoreceptors of the carotid and aortic bodies are tonically active at the oxygen tension present in the arterial blood of many normal men breathing room air at sea level. In resting human subjects, Meda (*2242* and *2243*) 1950 found that oxygen at normal barometric pressure caused a decrease in the heart rate of 3.7 to 11 percent. This reduction lasted only 10 to 35 minutes, even when oxygen breathing was continued. This bardycardia was not observed in subjects breathing an air mixture containing less than 50 percent of oxygen. The magnitude of the response was proportional to the percentage of oxygen in the air mixture.

To gain additional information on circulatory changes in normal men during inhalation of 100 percent oxygen at normal barometric pressure, Whitehorn, Edelmann, and Hitchcock (*2245*) 1946 have determined cardiac minute volume and systemic blood pressure under these conditions. The subjects of these experiments were young male subjects of 18 to 35 years of age in the basal state, lying quietly. Cardiac output was determined from ballistocardiograms. Cardiac minute volumes were consistently lower during inhalation of 100 percent oxygen as compared with determinations on the same subjects breathing air. Slowing of the heart was considered to be almost entirely responsible for the reduction in cardiac output during the first 10 minutes of oxygen breathing. On continued inhalation of 100 percent oxygen, reduction of stroke volume contributed to the total effect. Systolic blood pressure did not change but diastolic pressure

showed a slight but significant rise. The average diastolic pressure after 60 minutes of 100 percent oxygen breathing was 7 mm. Hg higher than the control value. The maintenance of the arterial blood pressure level in spite of reduced cardiac output was interpreted by the authors as evidence of an increase in the general peripheral vascular resistance. It was suggested that the cardiovascular effects of oxygen inhalation be kept in mind in conditions of hyperoxygenation of the blood, such as denitrogenation, and that they may play a part in the physiological responses to changes in barometric pressure.

In experiments on seven healthy young men, it was shown by Alella and Meda (*2238*) 1948 that administration of atropine prevented the decrease of pulse frequency caused by inhalation of 100 percent oxygen. Gijón and Lorenzo (*2241*) 1947 administered pure oxygen under normal barometric pressure to 30 healthy young guinea pigs for 48 to 72 hours. The electrocardiographic tracings did not reveal any symptoms of cardiac hypoxia under these conditions. There were no significant deviations in the glycogen content of the heart.

For a further study of cardiovascular changes occurring during oxygen breathing, a paper by Alveryd and Brody (*2239*) 1948 may be consulted.

2238. Alella, A. and E. Meda. Frequenza cardiaca durante la respirazione di O_2 nell'uomo ed importanza del vago. *Boll. Soc. ital. Biol. sper.*, 1948, *24:* 581–582. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 771. Abstr. [P]

2239. Alveryd, A. and S. Brody. Cardiovascular and respiratory changes in man during oxygen breathing. *Acta physiol. scand.*, 1948, *15:* 140–149.

2240. Dripps, R. D. and J. H. Comroe, Jr. The effect of the inhalation of high and low oxygen concentrations on respiration, pulse rate, ballistocardiogram and arterial oxygen saturation (oximeter) of normal individuals. *Amer. J. Physiol.*, 1947, *149:* 277–291. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 368. Abstr. [P]

2241. Gijón, F. R. and P. L. Lorenzo. El contenido de glicógeno del corazón de cobayas sometidos a respiración de oxígeno puro. *Farmacoter. act.* 1947, *4:* 394–398.

2242. Meda, E. I. Effetti della respirazione di miscele ricche di O_2 sull'apparato cardiovascolare dell'uomo. II. Variazioni elettrocardiografiche nell'uomo durante la respirazione di O_2. *Boll. Soc. ital. Biol. sper.*, 1950, *26:* 930–931. [P]

2243. Meda, E. Ricerche elettro cardiografiche durante la respiratione di miscele ricche di ossiggeno. *Riv. Med. aero., Roma,* 1950, *13:* 441–453. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1242.

2244. Whitehorn, W. V. and A. Edelmann. The cardiovascular response to the breathing of 100% oxygen at normal barometric pressure. U. S. NRC–CAM. *OEMcmr–74, C. A. M. rept. no. 474,* 13 September 1945. Abstr.

2245. Whitehorn, W. V., A. Edelmann, and F. A. Hitchcock. The cardiovascular responses to the breathing of 100 percent oxygen at normal barometric pressure. *Amer. J. Physiol.*, 1946, *146:* 61–65. [P]

4. EFFECTS ON THE BLOOD

Many workers have observed a decrease in the red blood count in subjects exposed to oxygen or hyperoxygenated air at normal atmospheric pressure for prolonged periods of time. Tinsley, Moore, Dubach, Minnich, and Grinstein (*2249*) 1949 subjected patients and normal persons to high oxygen concentrations for 8 to 14 days by means of a mask. Seventy percent oxygen was administered to the normal subjects for a period of 10 days. Results indicated that high oxygen tensions of inspired oxygen depress erythrocytogenesis in human subjects. The authors considered that their experiments provide further evidence that the oxygen tension of the arterial blood is one of the principal regulators of erythropoietic activity. These findings are in harmony with those of Cooperberg and Singer (*2246*) 1951 who investigated erythropoetic activity in the bone marrow of guinea pigs exposed to high oxygen tensions. In normal animals breathing high oxygen mixtures, there was a reticulocytopenia which was definitely caused by erythrocytic hypoplasia of the red bone marrow.

According to Donnell, Jensen, and Alt (*2247*) 1946, exposure of guinea pigs to intermittent high oxygen tension failed to depress erythropoiesis. These animals were intermittently exposed to 80 to 100 percent oxygen at normal atmospheric pressure for 57 days. The periods of exposure covered 6 hours a day, 6 days a week. There was no significant diminution in the erythrocyte counts and hemoglobin values in any of these animals.

For a further study of the relation of oxygen to erythropoiesis, a paper by Grant and Root (*2248*) 1947 may be consulted.

2246. Cooperberg, A. and K. Singer. The reaction of the bone marrow to high oxygen tension in normal and anemic guinea pigs. *J. Lab. clin. Med.*, 1951, *37:* 936–947.

2247. Donnell, W. S., A. V. Jensen, and H. L. Alt. Exposure of guinea pigs to intermittent high oxygen tension and its failure to depress erythropoiesis. *Proc. Soc. exp. Biol., N. Y.*, 1946, *63:* 64–66. [P]

2248. Grant, W. C. and W. S. Root. The relation of O_2 in bone marrow blood to posthemorrhagic erythropoiesis. *Amer. J. Physiol.*, 1947, *150:* 618–627.

2249. Tinsley, J. C., Jr., C. V. Moore, R. Dubach, V. Minnich, and M. Grinstein. The role of oxygen in the regulation of erythropoiesis. Depression of the rate of delivery of new red cells to the blood by high concentrations of inspired oxygen. *J. clin. Invest.*, 1949, *28:* 1412–1421. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1075. *Abstr. World Med.*, 1950, *8:* 343. [CH] [P]

5. EFFECTS UPON THE RESPIRATORY SYSTEM

Although there is lack of unanimity as to the effects of oxygen or hyperoxygenated air at normal barometric pressures upon respiration, the more reliable evidence indicates that oxygen administration does cause changes in breathing although these may not be large and may be masked by the techniques used in their measurements. The older literature indicates that in animals the respiratory minute volume is reduced by inhalation of oxygen, and in man, Patterson, Heyman, and Duke (*2258*) 1951 have found depression of pulmonary ventilation in patients with chronic pulmonary emphysema breathing 85 to 100 percent oxygen at normal barometric pressure.

Binet and Strumza (*2251*) 1947 recorded a drop in respiratory rhythm from 17 down to 14 per minute in dogs under chloralose anesthesia given pure oxygen at normal barometric pressure. The minute volume of respiration fell from 4.02 liters to 3.38 liters. This depressive effect of oxygen upon respiration was found to be transient. According to Gollwitzer-Meier (*2253*) 1948, breathing 100 percent oxygen by men (10 minutes) and narcotized dogs (6 to 7 minutes) was associated with an immediate drop in ventilation rate. Upon recovery on air, there was a gradual return within 1 to 7 minutes in man, while in dogs a hyperventilation was maintained for at least 6 minutes. Hypoventilation was not observed in dogs in which the sinus nerves were ligatured. The reaction of man to carbon dioxide in the inspired air before and after recovery from oxygen breathing indicates no change in the sensitivity of the respiratory system to carbon dioxide. These results are interpreted by the author on the theory that the chemoreceptors are inhibited by high oxygen pressure, but that the central control is stimulated. During the initial period of oxygen breathing, the chemoreflex drive is dominant but is soon overruled by the central drive, which persists and is slow to recover during the recovery period on air.

In 1948, Barach (*2250*) reviewed experimental and clinical studies on the effects of high concentrations of oxygen. Inhalation of 100 percent oxygen for periods under 7 hours has been shown to have no after-effects. The difficulty of obtaining high oxygen concentrations in oxygen tents or with nasal catheters minimizes the likelihood of oxygen poisoning by these methods of treatment. In administration of oxygen with masks, an intermittent schedule of administration is desirable.

Studies of pathological changes produced in the lungs by breathing oxygen or highly oxygenated air mixtures at normal barometric pressure have been described on pages 174 to 176 of the first volume of this Sourcebook. These pathological changes include inflammation, congestion, edema, atelectasis, fibrin formation, and consolidation of the lungs. There may be pneumonia of various types, bronchitis with bronchiectasis, and hypertrophy, hyperplasia, desquamation, and degenerative changes in alveoli. There may be also sclerotic changes with narrowing, thickening, and hyalinization of the pulmonary arteries.

Pulmonary edema and vascular congestion of the lungs have been described by Hemingway (*2254*) 1951 in guinea pigs subjected to almost pure oxygen at normal barometric pressure. There was little edema during the first 24 to 48 hours of thc high oxygen environment. Subsequently, edema progressively developed, causing death in 5 to 6 days. Kuhn and Pichotka (*2256*) 1948 exposed guinea pigs and rabbits to 90 to 98 percent oxygen mixtures at normal barometic pressure for 60 to 122 hours. These animals showed a hyalinelike mcmbrane in the lungs as well as necrosis of the bronchial epithelium. There was an alveolar exudate consisting of fibrin and leucocytes. In an experimental investigation on 3 adult and 9 infant guinea pigs, exposed to 98 percent oxygen at normal barometic pressure for several days, Bruns and Shields (*2252*) 1951 found a hyalinelike membrane in the lungs after 50 to 64 hours. The general pathological findings in all animals dying in high concentrations of oxygen were paradoxically those of anoxia. The authors carried out their investigations in an attempt to explain the formation of hyalinelike membranes in the lungs of stillborn infants and infants dying neonatally.

In a study of the pathogenesis of pulmonary damage caused by breathing oxygen at normal barometric pressure, Ohlsson (*2257*) 1947 reported that the pulmonary damage in oxygen poisoning at 1 atmosphere seems to be caused by a lesion of the capillary wall. The damaging effects of oxygen are considerably higher in experiments in which 3 to 3.5 percent carbon dioxide is added to the respiratory mixture. The author considers that the decrease in vital capacity observed in high oxygen breathing is due partly to the dilating effect of the oxygen on the pulmonary vessels and partly to an exudation into thc pulmonary tissue caused by oxygen at high partial pressure. The author considers that there is no experimental basis for the view that pulmonary damage in oxygen poisoning is produced by a direct effect of oxygen in the pulmonary tissue. He suggests rather that the pulmonary damage in oxygen poisoning is caused by disturbance of the carbon dioxide transport in the venous blood.

For an experimental study on the resistance of animals to chronic oxygen poisoning, a paper by Hempleman (*2255*) 1951 may be consulted.

2250. Barach, A. L. Oxygen poisoning. pp. 303–309 in: *Physiologic therapy in respiratory diseases.* Second edition. Philadelphia, J. B. Lippincott Co., 1948, 408 pp.

2251. Binet, L. and M. V. Strumza. Sur l'effet dépresseur respiratoire de l'inhalation brusque d'oxygène pur. *C. R. Soc. Biol., Paris,* 1947, *141:* 3–5. [P]

2252. Bruns, P. D. and L. V. Shields. The pathogenesis and relationship of the hyalinelike pulmonary membrane to premature neonatal mortality. *Amer. J. Obstet. Gynec.,* 1951, *61:* 953–965. [P]

2253. Gollwitzer-Meir, K. Über die Wirkung der Sauerstoffatmung auf das Atemzentrum und über ihre Nachdauer. *Pflüg. Arch. ges. Physiol.,* 1947, *249:* 32–43. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 629. Abstr.

2254. Hemingway, A. Effect of hypoxia and oxygen poisoning on pulmonary edema. *Fed. Proc. Amer. Soc. exp. Biol.,* 1951, *10:* 62.

2255. Hempleman, H. V. The reistance of animals to chronic oxygen poisoning. Gt. Brit. MRC–RNPRC, UPS. Royal naval physiological laboratory, Alverstoke. *R. N. P. 51/652, U. P. S. 127,* 8 pp. [P]

2256. Kuhn, H. A. and J. Pichotaka. Über die Morphogenese der Lungenveränderungen bei der Sauerstoffvergiftung. *Arch. exp. Path. Pharmak.,* 1948, *205:* 667–683. [P]

2257. Ohlsson, W. T. L. A study of oxygen toxicity at atmospheric pressure with special reference to the pathogenesis of pulmonary damage and clinical oxygen therapy. *Acta med. scand.,* 1947, Suppl., *190:* 1–93. [P]

2258. Patterson, J. L., Jr., A. Heyman, and T. W. Duke. The cerebral circulation and metabolism in chronic pulmonary emphysema with observations on the effects of inhalation of oxygen. U. S. Navy. NATC, Pensacola, Fla. School of aviation medicine. *Project NM 001 050.01.02,* 26 July 1951, 11 pp.

6. EFFECTS ON METABOLISM

Analysis of the literature on the effects of oxygen and hyperoxygenated air at normal barometric pressure upon the metabolic processes reveals no consistent and dependable evidence that breathing oxygen-rich air or pure oxygen causes any change in metabolism manifested by alteration in exchange of respiratory gases. Most reports support the view that the respiratory exchange is not a function of oxygen tension except under those conditions in which the oxygen tension falls below normal. A number of metabolic responses to high oxygen tension may be discerned, however. Mann and Quastel (*2264*) 1946 found that the respiration of minced brain tissue falls off to a greater extent in the presence of oxygen than in the presence of air, particularly when the respiration of the brain tissue takes place in the presence of glucose, sodium lactate, or sodium pyruvate. The respiration of minced brain in the presence of sodium succinate appears not to be so oxygen sensitive. The evidence points to the pyruvate oxidizing system as constituting that part of the brain respiratory system most sensitive to oxygen. Mann and Quastel suggest that pyruvate oxidase is the substance which is poisoned by high tensions of oxygen.

Regarding the effect of prolonged inhalation of oxygen upon the emptying time of the stomach and speed of intestinal absorption of isotonic solutions of glucose in the rat, Cordier and Chanel (*2261*) 1950 found no changes in these functions in rats kept in pure oxygen at atmospheric pressure. It appears that inhalation of oxygen may bring about improvement in patients with impaired liver function. Kaufman, Hollo, Rosenthal, Stone, Beck, and Fink (*2263*) 1950 found in patients with depressed hepatic function that breathing of 10 percent oxygen with 90 percent nitrogen for 35 minutes impaired BSP excretion to a significant degree. Breathing 100 percent oxygen for 4 hours improved in certain cases the excretion of the dye. Other liver function tests carried out in combination with hypoxia or hyperoxia gave inconclusive results.

Binet and Bargeton (*2260*) 1941 have reported experiments on the action of oxygen inhalation on muscular work in rats. The animals were anesthetized and the gastrocnemius exposed and stimulated electrically. The work level of the stimulated muscle was augmented when the rats breathed oxygen. In human subjects, Asmussen, von Döbeln, and Nielsen (*2259*) 1948 found that breathing pure oxygen increased the capacity for work. In this study healthy males exercising on a bicycle ergometer were subjected to acute changes in oxygen tension of the inspired air. The maximum blood lactate concentration was practically the same as under normal air conditions.

For further studies of the effects of high oxygen tensions on metabolism, papers by the following may be consulted: Dediulin (*2262*) 1949, Massey and Rogers (*2265*) 1950, and Ruiz Gijon and Lopez Lorenzo (*2266*) 1947.

2259. Asmussen, E., W. von Döbeln, and M. Nielsen. Blood lactate and oxygen debt after exhaustive work at different oxygen tensions. *Acta physiol. scand.,* 1948, *15:* 57–62. [P]

2260. Binet, L. and D. Bargeton. Action de l'inhalation de mélanges riches en oxygène sur le travail musculaire fourni par le rat normal et par le rat décapsulé. *C. R. Soc. Biol., Paris,* 1941, *135:* 1523–1526. [P]

2261. Cordier, D., and J. Chanel. Influence de l'inhalation prolongée d'oxygène sur la vitesse du transit gastrique et l'absorption intestinale des solutions isotoniques de glucose chez le rat. *C. R. Soc. Biol., Paris,* 1950, *144:* 1373–1374. [P]

2262. Dediulin, I. M. K probleme kislotno-shchelochnogo ravnovesiia v organizme cheloveka pri ponizhennom i pri povyshennom partsial'nom davlenii kisloroda.

[Acid-base equilibrium in the human organism in increased and decreased oxygen pressure.] pp. 44–45 in: *Gipoksiia*, Kiev, Akad. Nauk Ukr. SSR., 1949, 415 pp.

2263. **Kaufman, P., J. Hollo, J. Rosenthal, J. Stone, R. D. Beck, and V. Fink.** The effect of 10% and 100% oxygen inhalation on certain liver-function tests. *New Engl. J. Med.*, 1950, *242:* 90–92. [P]

2264. **Mann, P. J. G. and J. H. Quastel.** Toxic effects of oxygen and of hydrogen peroxide on brain metabolism. *Biochem. J.*, 1946, *40:* 139–144. [P]

2265. **Massey, V. and W. P. Rogers.** Effects of oxygen carriers and oxygen tensions on fluoroacetate inhibition of citrate utilization. *Nature, Lond.*, 1950, *166:* 951.

2266. **Ruiz, G. J. and P. Lopez Lorenzo.** El contenido de glicógeno del corazón de cobayas sometidos a respiración de oxígeno puro. *Farmacoter. act.*, 1947, *4:* 394–398. [P]

2267. **Stevenson, I. P. and L. Smith.** The influence of oxygen tension upon the respiration of rat kidney slices. *Arch. Biochem.*, 1948, *17:* 61–73. [P]

B. EFFECTS OF OXYGEN TENSION IN EXCESS OF ONE ATMOSPHERE

1. GENERAL STUDIES

If oxygen is breathed at a sufficiently high pressure above 1 atmosphere for a sufficient length of time, generalized convulsions supervene. The requisite length of exposure varies inversely with the partial pressure of oxygen breathed. The cause of the convulsions still remains unclear in spite of the large number of experimental investigations that have been brought to bear upon this important subject. After the bibliographical lists of this volume of the Sourcebook had been compiled, and therefore too late for inclusion, two important papers on oxygen toxicity appeared in the March 1953 issue of the Journal of Applied Physiology. The first of these, by C. J. Lambertsen, R. H. Kough, D. Y. Cooper, G. L. Emmel, H. H. Loeschke, and C. F. Schmidt, is entitled "Oxygen Toxicity; Effects in man of oxygen inhalation at 1 and 3.5 atmospheres upon blood gas transport, cerebral circulation, and cerebral metabolism." The second paper, by C. J. Lambertsen, M. W. Stroud, R. A. Gould, R. H. Kough, J. H. Ewing, and C. F. Schmidt, is entitled "Oxygen toxicity: Respiratory responses of normal men to inhalation of 6 to 100 percent oxygen under 3.5 atmospheres pressure." These papers should be consulted for excellent bibliographical lists, critical discussions of previous research, and significant experimental contributions. Lambertsen and coworkers point out that, at present, the explanation of the convulsions resulting from exposure to high oxygen pressures appears to rest upon one or more of the following: (1) a direct toxic effect of high oxygen pressures upon certain constituents of brain cells; (2) an accumulation of carbon dioxide in toxic quantities in the central nervous system because of breakdown in the normal transport function of hemoglobin for this gas; and (3) changes in the cerebral circulation. They conclude that central accumulation of carbon dioxide on breathing oxygen at increased ambient pressures does not contribute to the toxicity of oxgyen, but rather may reduce indirectly the exposure of brain tissue to toxic levels of oxygen tension by producing hyperventilation and cerebral vasoconstriction.

For three reports from overseas giving general material on the toxic action of oxygen, papers by the following should be consulted: Ruiz Gijon (*2272*) 1951; Spurway-Haldane and Haldane (*2274*) 1945; and Tailliez, Dumas, Cousteau, Alinat, and Devilla (*2275*) 1949.

A particularly significant series of papers on oxygen poisoning in man is that presented by Donald (*2270*) 1946 and (*2268* and *2269*) 1947. The first of these gives a full explanatory and historical background of the subject of oxygen poisoning in man. The first series of experiments reported by Donald (*2268*) was carried out to determine the oxygen tolerance of a group of healthy male subjects at a fixed oxygen tension corresponding to 3.7 atmospheres absolute. These experiments were carried out in a pressure chamber of 100-cubic-foot capacity and all subjects breathed oxygen at pressure until acute symptoms developed. Symptoms in 36 subjects included prolonged "dazzle," and severe spasmodic vomiting to severe lip twitching. The most striking finding was an enormous variation in oxygen tolerance in this group of human subjects. The subjects were also exposed to high oxygen tension in wet runs in a diving tank. The respiratory apparatus worn was a modification of the Davis submarine escape apparatus. A light rubberized canvas suit with a soft helmet was worn. The subjects breathed oxygen at atmospheric pressure for 10 minutes before arriving at the experimental depth. The compression time was 90 seconds. The temperature of the water was 65° F. The first series of experimental dives was to 50 feet (2.5 atmospheres absolute). One hundred subjects were used. If a subject convulsed or had other severe symptoms, he was hauled out immediately. Out of 100 subjects, 26 had convulsions, 24 had other symptoms, and 50 had no symptoms. A series of dives was undertaken to compare the tolerance of subjects in compressed air and under water at 60 feet and 90 feet of sea water. The experimental data indicated that tolerance is greatly decreased when under water as compared with dry runs. After a large number of experiments, a new factor became increasingly evident. It became clear that the tolerance of individual subjects varied from

day to day, and it was impossible to plot a curve for a single subject. The findings seem to indicate that diving on oxygen to any toxic pressure involves a risk impossible to determine in advance, even if the diver's tolerance has been previously measured. In wet oxygen dives carried out by groups of subjects at 50, 60, 70, 80, 90, and 100 feet, the toxic effects became greater as the depth increased. The variability of the group was found to be independent of depth. In a series of experiments to discover at what pressure under water oxygen begins to cause toxic nervous symptoms, the author elicited no symptoms at 25 feet. It was surprising to find oxygen convulsions at as low a pressure as 33 feet of sea water. Tolerance to oxygen was markedly diminished by vigorous work consisting of lifting a large bag of weights by a pulley. The physiological basis for this effect is not definitely known.

The signs and symptoms of oxygen poisoning have been investigated by Donald (*2269*) 1947. Facial pallor occurs within a few minutes after the beginning of the exposure. Fasciculation of the lips or face is often seen early in the experiment and sometimes throughout the exposure. This is attributed partially to fatigue from the mouthpiece. Some subjects show facial perspiration, and in some cases there is generalized sweating associated with more severe stress. Salivation seems to increase, but this is probably a reflex response to the presence of the mouthpiece. There may be nausea, vertigo, malaise, apprehension, or choking sensations. Palpitations may also occur. As the intoxication becomes more intense, there are changes in mood. Severe irrational apprehension, sometimes amounting to acute terror is observed, and sometimes the subjects complain of feeling "far away." Some subjects fall asleep and can be aroused only with difficulty. Visual or auditory hallucinations are late symptoms. Patients complain of flashes of light in the center of the visual field, halos around objects, lateral movement of images, micropsia, and changes in apparent brightness of illumination. There may be a sense of ringing in the ears, deafness, or hyperacuity. Unpleasant tastes or odors are complained of in the wet dives, but not in the dry environment. Constriction of the visual fields is gradual. Shortly before the convulsive attack, there is definite twitching of the lips which is powerful and sustained. These convulsive movements of the lips pass into generalized jactitations. Occasionally isolated twitching of the arm, leg, or trunk occurs. There may be rapid, panting movements. Convulsive attacks due to oxygen poisoning were found to be about 2 minutes in duration and only one attack usually resulted if air was given immediately. On one occasion when air was not given (by accident), another attack occurred 30 seconds later. The attack is followed by confusion, dissociation, headache, nausea, and vomiting. A majority of the subjects in the post-convulsive period were subdued and ataxic, and usually fell asleep after 15 minutes. There tended to be amnesia for the experience and the subjects complained of stiffness in the trunk. In some subjects, the onset of air breathing seemed to bring on convulsions. To avoid these convulsions associated with transfer from oxygen to air, subjects were not decompressed until symptoms were gone. In the wet dives, 9.2 percent of the subjects experienced convulsions, 60.6 percent showed lip twitching, and vertigo was experienced in 8.8 percent. Nausea was recorded in 8.3 percent, respiratory disturbances in 3.8 percent, general twitching in 3.2 percent, drowsiness and confusion in 3.2 percent, visual disturbances in 1 percent, and acoustic hallucination in 0.6 percent. Regarding pulmonary symptoms, Donald found no irritation of the lungs after wet dives at 50 feet for 30 minutes. At depths greater than 30 feet, nervous symptoms necessitated termination of the dive long before any pulmonary irritation occurred. X-rays taken of the exposed men over periods of 2 years yielded no positive findings. In some cases, the pulse slowed after long exposures to 60 feet, and some of the convulsed subjects did not recover normal rate until several hours after exposure. There was no relation between bradycardia and tolerance. X-rays revealed no cardiac enlargement. Within a 3-year period, no aftereffects were observed in neurological integrity, intellectual ability, or personality. No unusual reflex effects were observed acutely at 60 and 90 feet dry runs. Some subjects showed pupillary dilation at the end of exposure. Exposure to oxygen at 120 feet had no immediate effects upon the electroencephalogram. At no time was any attack akin to petit mal observed either clinically or electrically. Donald concluded from his studies that variations of tolerance between individuals and impairment of tolerance with work and underwater conditions all make diving on pure oxygen at depths greater than 25 feet of sea water a hazardous undertaking. It is emphasized that no signs or symptoms can be given that will insure a timely cessation of oxygen breathing in all cases.

Experimental studies of oxygen poisoning at raised atmospheric pressures have been reported by Pichotka and Kühn (*2271*) 1947. Guinea pigs and rabbits breathing oxygen at 3.5 to 5.8 atmospheres died within a period of 1 hour. Pathological changes in the lungs and liver are described.

Schaefer, Alvis, Webster, and Willmon (*2273*) 1949 have investigated symptoms produced by ex-

posure of underwater swimmers to oxygen during swimming trials in a tank under pressure. Subjects swam at a rate of about 0.9 mile an hour. Fifty trials were made. The average exposure time to produce symptoms was 61.7 $\pm$21.5 minutes at a depth of 22.1 $\pm$9.9 feet. The authors concluded that at 10 feet, 6 to 29 percent of the men would be expected to show symptoms. At 20 feet, symptoms would be shown by 10 to 33 percent. At 30 feet, symptoms would be found in 15 to 39 percent, while at 40 feet, 20 to 46 percent would show symptoms. At 50 feet, 26 to 55 percent would show symptoms, and at 60 feet, 34 to 65 percent of the subjects would be expected to complain of symptoms.

2268. Donald, K. W. Oxygen poisoning in man. *Brit. med. J.*, 1947, *1:* 667–672. *Arch. Mal. Prof.*, 1948, *9:* 83–85. *J. industr. Hyg.*, 1947, *29:* abstract section: 100. [P]

2269. Donald, K. W. Oxygen poisoning in man. II. Signs and symptoms of oxygen poisoning. *Brit. med. J.*, 1947, *1:* 712–717. [P]

2270. Donald, K. W. Oxygen poisoning in man. Gt. Brit. Royal Navy, Admiralty experimental diving unit, H. M. S. *Vernon. Report No. XVI,* 1946, 208 pp. [P] [R]

2271. Pichotka, J. and J. A. Kühn. Experimentelle und morphologische Untersuchungen zur Sauerstoffvergiftung. *Arch. exp. Path. Pharmak.*, 1947, *204:* 21–36. [P]

2272. Ruiz, G. J. La accion toxica del oxigeno. *Med., Madrid,* 1951, *18:* 264–281.

2273. Schaefer, K. E., H. J. Alvis, A. P. Webster, and T. L. Willmon. Studies of oxygen toxicity. 1. Preliminary report on underwater swimming while breathing oxygen. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 015.03.01,* 22 October 1949, 9 pp.

2274. Spurway-Haldane, H. and J. B. S. Haldane. La vie humaine à haute pression. *C. R. Soc. Biol., Paris,* 1945, *139:* 1062–1063.

2275. Tailliez, P., F. Dumas, J. Y. Cousteau, J. Alinat, and F. Devilla. Intoxication par l' oxygène. pp. 52–54 in: *La plongée en scaphandre.* Paris, Editions Elzevir, 1949, 119 pp.

2. CONVULSIONS AND OTHER DISTURBANCES OF THE CENTRAL NERVOUS SYSTEM

In studies reported by Yarbrough, Welham, Britton, and Behnke (*2289*) 1947, it was confirmed that naval personnel given oxygen under pressure supported dry chamber runs for a longer period than underwater runs. Subjects at rest tolerated a simulated depth of 60 feet with oxygen in the dry chamber for 2 hours without neurological symptoms. At the same depth under water at rest, 32 out of 107 exposures had to be terminated prior to 60 minutes. The average time of termination was 30 minutes, the range being 8 to 58 minutes. In 2 subjects convulsive seizures occurred, 1 after 13 minutes and 1 after 24 minutes. At a depth of 80 feet, 74 out of 99 exposures ended prior to 60 minutes. At a depth of 100 feet, 43 out of 46 exposures ended prior to 60 minutes. The authors concluded that moderate work can be done safely at 30 feet or less. At this depth in 35 exposures, symptoms were manifest in 2 men at 87 and 111 minutes. At 40 feet, symptoms occurred in 19 out of 71 exposures prior to 2 hours. At 50 feet, symptoms occurred in 3 out of 5 exposures. Symptoms responsible for termination of 168 quiescent exposures in dry and wet chambers at 60, 80, and 100 feet were nausea, twitching, vertigo, visual disturbances, restlessness, irritability, numbness, and convulsions. The latter were reported in 4 percent of the subjects. The symptoms were found rapidly to disappear when air was substituted for oxygen.

Convulsions induced in psychotic patients by oxygen inhalation at increased ambient pressures have been described and studied by Gould, Lambertsen, Kough, Stroud, Ewing, and Frehan (*2284*) 1951. This report is part of a broad study of the effects of oxygen at high pressure. As part of this investigation, the possibilities of oxygen convulsions as a new form of convulsive psychiatric therapy are being studied. Kough, Cooper, Emmel, Louschcke, Lambertsen, and Schmidt (*2285*) 1950 have measured the effects of high tensions of inspired oxygen on the cerebral blood flow, cerebral oxygen consumption, and cerebral vascular resistance in three groups of healthy young men. The original source may be consulted for a tabulation of results.

For experimental studies on transient and permanent aftereffects of exposure of rats to oxygen at high pressures, three papers by Bean and Siegfried (*2276* and *2277*) 1945 and (*2278*) 1946 should be consulted. Young adult, unanesthetized rats were subjected to oxygen at 65 lbs. gage pressure in short, single, or successive exposures (*2276*). The chamber temperature was maintained at 24° C., and carbon dioxide was absorbed. The acute reactions occurring during compression or immediately after the acute reactions included stupor, coma, catatonia, hyperexcitability, hypotonia, and hypertonia, as well as tonic convulsive reactions, motor dysfunctions, and dyspnea. Recovery was rarely immediate even after single exposures. After apparent complete recovery from acute reactions following single exposure, alterations persisted for some time. Chronic effects were characterized by spastic motor paralysis, which in the less severe cases involved only the forelegs, but which in more pronounced cases affected almost the entire body musculature. The chronic effects were induced by successive exposures given 2 to 4 times a day and were usually permanent. The animals showed a wide individual variation in sus-

ceptibility to the chronic effects (*2276* and *2277*). Permanent motor paralysis supervened in some animals that had failed to show acute reactions. The occurrence of convulsive attacks or lesser disturbances during either the exposure to or decompression from oxygen at high pressure was not an essential prelude to the production of the permanent motor disabilities by successive exposures. The susceptibility of the animals to the toxic action of oxygen at high pressure was progressively increased with successive exposures, but this increase did not continue indefinitely. After a plateau had been attained, the susceptibility remained relatively constant unless the program of exposures was altered. The authors viewed the reactions occurring during exposure to and decompression from oxygen at high pressure, as well as the more transient of the acute postdecompression reactions, as due to the toxic influence of an accumulation of endogenous carbon dioxide in the tissues, increased tissue acidity, and a direct action of oxygen at high pressure on tissue enzymes. The more persistent of the acute postdecompression effects are attributed by the authors to more slowly reversible alterations in the tissues, conceivably a slowly reversible tissue injury by these same transient toxic agents. In regard to the chronic postdecompression effects, manifest by permanent motor disability, the authors consider that irreversible tissue damage and degenerative changes within the central nervous system have been induced by the same toxic agents. The nature of the permanent disability points to the upper motor neuron as the permanent site of disturbance, although other portions of the central nervous system are possibly also involved. Bean and Siegfried (*2278*) 1946 have pointed out that some rats exposed to oxygen at 65 pounds gage pressure for 10 to 25 minutes, 2 to 4 times a day for many days, show permanent motor disability characterized by chronic, spastic paralysis involving the limbs and body musculature for as long as 18 months after exposure. Eight-day-old chicks exposed to oxygen at 90 and 65 lbs. gage pressure in a similar manner over a period of days were similarly affected, and the disability thus induced persisted into adult life.

The syndrome of oxygen poisoning in cats has been reported by Gersh (*2280*) 1944 and (*2281*) 1945. These animals were exposed to pressures of 60, 70, 90, or 100 pounds gage pressure in oxygen. The cats appeared quiet until a few minutes before the onset of the motor seizure. They then showed restlessness and began to explore the inside of the pressure tank. The pupils became widely dilated, and stringy saliva drooled from the mouth. There was piloerection and panting. Just before the onset of the seizure, the muscles of the ears, forelegs, and neck began to twitch. Generalized convulsive movements were initiated with explosive violence, and continued during decompression and even 3 to 10 minutes after removal of the animal from the tank. Frequently, there was micturition and defecation. As the involuntary movements subsided, the animals showed exaggerated tone in the antigravity or in flexor muscles. The animals were insensitive to visual, auditory, or painful stimuli, and the pupils were widely dilated. As sensory functions gradually returned, the cats became difficult to arouse to motor activity. When the animals were subjected repeatedly to oxygen seizures, there were signs of cumulative neurological damage manifested by deterioration of hopping, placing, and dropping reactions, especially in the forelegs. There was also persistent increase in extensor tone. These changes tended to disappear after prolonged rest. The author concluded that the motor seizures originate in the cerebral cortex in which the neurons are probably most sensitive to the toxic action of oxygen. This conclusion and interpretation is supported by the electroencephalographic findings. Gersh (*2281*) 1945 and Gersh and Cohn (*2282*) 1944 found that the brain-wave pattern during oxygen convulsions in the cat resembles that observed in other well-defined clinical and experimentally induced seizures. Slow brain waves appear before the onset of the seizure and become progressively more permanent, alternating with periods of high frequency activity and with phases of exhaustion during which no activity is elicited. Drugs most effective in delaying the seizures were depressants of central nervous system activity. Pathological changes in cats repeatedly exposed to oxygen under pressure were found to be slight.

Stein and Sonnenschein (*2288*) 1950 have reported on the electrical activity and oxygen tension of the brain during hyperoxic convulsions in cats. In animals exposed to 100 percent oxygen at an increasing pressure of 2½ lbs. per minute, it was found that convulsions appeared within 2 to 10 minutes after a pressure of 75 lbs. gage pressure had been reached. The seizures lasted for a few seconds to 2 minutes, followed by a quiet phase of 1 to 5 minutes before the next seizure started. Twenty to forty such seizures may occur in one-half to 1 hour at a sustained pressure of 45 lbs. gage pressure. After 1 hour, brain activity diminished and disappeared. During the seizures and the period of decreased activity, the electroencephalogram showed no marked changes in rate or rhythm. The

authors concluded that the convulsions may start elsewhere than in the cerebral cortex.

Gersh, Davies, and Larrabee (*2283*) 1945 found in cats in an atmosphere of oxygen under high pressure that the "oxygen tension" value of the cerebral cortex rises very early and then falls abruptly to a plateau which slopes to a slightly lower value at the time of death of the animal. Cortical damage may occur at the time of the sharp peak in oxygen tension, and after a latent period becomes manifest in the characteristic convulsive seizure. As stated, drugs which depress the central nervous system showed some effect in reducing the incidence or severity of the convulsions. Pfeiffer and Gersh (*2286*) 1944, in a study on 250 cats, investigated 48 drugs. Of these, only a few compounds were found to be effective. These were glutamic acid, lactic acid, sodium lactate, ammonium chloride, cysteine, and central nervous system depressants. All drugs depressing the central nervous system showed some degree of activity, but the short-acting barbiturates were the most effective. When daily oxygen convulsions were prevented with pentobarbital sodium, temporary functional impairment of the central nervous system occurred. Metrazol, mecholyl, carbon dioxide, and sodium bicarbonate shortened the preconvulsive period. Atropine and methylene blue increased the severity of the convulsions. Various combinations of effective drugs were tried, but the only evidence of possible synergistic action was found with combinations of pentobarbital and lactic acid or sodium lactate.

Degenerative changes induced in the central nervous system of albino rats by exposure to oxygen at high pressure have been described by Siegfried and Bean (*2287*) 1946. In these experiments, albino rats were exposed to oxygen at increased pressure, usually 65 lbs. gage pressure, for short periods from 10 to 25 minutes, 2 to 4 times a day, over a period of time necessary to produce definite permanent motor impairment. Because of wide variations in individual susceptibility, the program of exposures varied considerably for different animals. Decompression was such as to preclude the possibility of bubble formation. Following the last exposure, an interval of about 14 days was permitted to elapse to allow degenerative changes to become demonstrable histologically. The animals were then sacrificed, and brain and cord preparations examined. Histological examination revealed numerous sites of degenerative changes, varying in degree from slight to severe. The most common and permanent degeneration was found in the corticospinal tract. Less permanently and less consistently, degenerative involvement was found in the fasiculus gracilis and also the spinocerebellar tracts, the brachiumpontis, the cerebral peduncles, and corpus callosum. In a few preparations, there was evidence of optic-nerve involvement. The severity and extent of the histopathological lesions were not uniformly commensurate with the severity and extent of the motor dysfunction manifest by the animal prior to sacrifice. These results indicate a widespread deleterious effect of oxygen at these pressures on the central nervous system.

For a further study of the nervous system symptoms of oxygen poisoning, a note by Culpin (*2279*) 1947 may be consulted.

2276. Bean, J. W. and E. C. Siegfried. Transient and permanent aftereffects of exposure to oxygen at high pressure. *Amer. J. Physiol.*, 1945, *143:* 656–665. [P]

2277. Bean, J. W. and E. C. Siegfried. Permanent motor disabilities induced by successive exposures to oxygen at high pressures. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 6.

2278. Bean, J. W. and E. C. Siegfried. Chronic motor disability resulting from repeated exposure to oxygen at high pressure. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 6.

2279. Culpin, M. Oxygen poisoning in man. *Brit. Med. J.*, 1947, *2:* 70–71.

2280. Gersh, I. The syndrome of oxygen poisoning in cats. U. S. Navy. NMRI. *Project X–192, Rept. no. 1,* 30 October 1944, 9 pp. [P]

2281. Gersh, I. Syndrome of oxygen poisoning in cats. *War Med., Chicago,* 1945, *8:* 221–228.

2282. Gersh, I. and R. Cohn. Changes in brain potentials during convulsions induced by oxygen under pressure. U. S. Navy. NMRI. *Project X–192, Rept. no. 4,* 30 October 1944, 5 pp. [P]

2283. Gersh, I., P. W. Davies, and M. G. Larrabee. "Oxygen tension" of the cerebral cortex of cats during oxygen poisoning. U. S. Navy. NMRI. *Project X–192, Rept. no. 6,* 7 May 1945, 5 pp. [P]

2284. Gould, R. A., C. J. Lambertsen, R. H. Kough, M. W. Stroud, J. H. Ewing, and F. A. Freyhan. Convulsions induced in psychotic patients by oxygen inhalation at increased ambient pressures (motion picture). *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 53.

2285. Kough, R. H., D. Y. Cooper, Jr., G. L. Emmel, H. H. Loeschcke, C. J. Lambertsen, and C. F. Schmidt. Effect of inhalation of oxygen at high partial pressure upon cerebral circulation and cerebral oxygen consumption in man. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 72.

2286. Pfeiffer, C. C. and I. Gersh. The prevention of the convulsions of oxygen poisoning by means of drugs. U. S. Navy. NMRI. *Project X–192, Rept. no. 2,* 30 October 1944, 7 pp. [P]

2287. Siegfried, E. C. and J. W. Bean. Degenerative changes induced in the C. N. S. of albino rats by exposure to O_2 at high pressure. *Fed. Proc. Soc. exp. Biol.*, 1946, *5:* 95.

2288. Stein, S. N. and R. R. Sonnenschein. Electrical activity and oxygen tension of brain during hyperoxic convulsions. *J. Aviat. Med.*, 1950, *21:* 401–404. [P]

2289. Yarbrough, O. D., W. Welham, E. S. Britton, and A. R. Behnke. Symptoms of oxygen poisoning and limits of tolerance at rest and at work. U. S. Navy. Naval gun factory, EDU. *Project X–337 (Sub. no. 62) Rept. no. 1,* January 1947, 9 pp.

3. EFFECTS ON RESPIRATION

In a consideration of the possible harm from inhalation of oxygen at high pressure, Comroe and Dripps (*2290*) 1950 draw attention to the occurrence of oxygen apnea in subjects whose respiratory center is no longer regulated normally by carbon dioxide and who have no important reflexes other than chemoreceptor reflexes maintaining respiration. Lambertsen, Cooper, Emmel, Loeschcke, Kough, and Schmidt (*2293*) 1950; Lambertsen, Emmel, Cooper, Loeschcke and Kough (*2294*) 1950; and Lambertsen, Kough, Cooper, Emmel, Loeschcke, and Schmidt (*2295*) 1950 have reported the effects in man of inhalation of oxygen at high partial pressure upon oxygen content, carbon dioxide content, oxygen and carbon dioxide tensions, and pH in arterial and internal jugular blood. In these experiments significant changes were produced by oxygen at 3.5 atmospheres. At 3.5 atmospheres the arterial plasma oxygen content almost met cerebral oxygen requirements as indicated by the near arterial level of internal jugular hemoglobin saturation. Hemoglobin base available for carbon dioxide transport by reduction of hemoglobin decreased 60 percent, producing an 8-millimeter increase in the arteriovenous carbon dioxide tension difference. A rise in venous oxygen tension reflects an increased brain-tissue carbon dioxide tension which probably contributed to the decreased arterial carbon dioxide tension by an increased pulmonary ventilation observed in subsequent experiments. Pulmonary irritation by oxygen has not been excluded as a factor in the respiratory stimulation. The small increase in venous carbon dioxide tension indicates that retention of carbon dioxide in the brain during exposure to oxygen at high partial pressure is not an important factor in acute oxygen poisoning.

Gersh (*2291*) 1944 has investigated pneumothorax and extrapulmonic emphysema in cats exposed to oxygen under pressure. Gross and microscopic observations on the lungs and associated structures of cats subjected to oxygen at high pressures showed spontaneous atelectasis. The primary defect appears to be a rupture of a few alveoli into the retropleural connective tissue in the manner of a one-way valve. The next state is the escape of this gas into the hilus, posterior mediastinal tissue and the pleural spaces. The final stage takes place during decompression and is due to the expansion of the gases in these sites, with a coincident compression of the lung. Spontaneous atelectasis was observed only in old cats.

Methods for the estimation of the tissue fluid were utilized by Hawkinson and Gersh (*2292*) 1945 in the investigation of pulmonary edema, which develops on exposure to oxygen at 1 atmosphere and at high pressures. The outstanding pulmonary change resulting from exposure of guinea pigs to 8 atmospheres of oxygen is a significantly decreased chloride concentration of the tissue fluid and of the lung as a whole without any important variation in the water content. This unexpected finding is interpreted by the authors to mean that a change in permeability of cells in the lungs has taken place as a result of the toxic action of oxygen under pressure. In contrast to the high-pressure experiments, exposure of guinea pigs to 1 atmosphere of oxygen resulted in an increased chloride and water content consistent with pulmonary edema.

2290. Comroe, J. H. and R. D. Dripps. Possibilities of harm from the inhalation of oxygen. pp. 58–75 in: *The physiological basis for oxygen therapy.* Springfield, Charles C. Thomas, 1950, 85 pp. [D]

2291. Gersh, I. Pneumothorax and extrapulmonic emphysema in cats exposed to oxygen under pressure. U. S. Navy. NMRI. *Project X–192, Rept. no. 5,* 30 October 1944, 4 pp. [P]

2292. Hawkinson, G. E. and I. Gersh. Biochemical study of pulmonary edema of guinea pigs exposed to high oxygen atmospheres. U. S. Navy. NMRI. *Project X–192, Rept. no. 7,* 24 September 1945, 7 pp. [P]

2293. Lambertsen, C. J., Y. D. Cooper, G. L. Emmel, H. H. Loeschcke, R. H. Kough, and C. F. Schmidt. Some observations on the role of carbon dioxide in acute oxygen toxicity at 3½ atmospheres inspired oxygen tension. *Amer. J. med. Sci.,* 1950, *219:* 581–582.

2294. Lambertsen, C. J., G. L. Emmel, D. Y. Cooper, H. H. Loeschcke, and R. H. Kough. Effects of inhalation of oxygen at high partial pressures upon arterial and internal jugular blood gas content, tension and pH. *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 73.

2295. Lambertsen, C. J., R. H. Kough, D. Y. Cooper, G. L. Emmel, H. H. Loeschcke, and C. F. Schmidt. Some effects upon man of oxygen inhalation at high partial pressures. *XVIII. Intern. physiol. Congr.,* 1950, 322–323.

4. EFFECTS ON METABOLISM

Dickens (*2297*) 1946 has reported that the respiration of brain tissue is slowly and irreversibly poisoned by exposure of the isolated tissue to oxygen at high pressure. Even at 1 atmosphere, very slow poisoning by oxygen occurs, and above this pressure the rate of poisoning steadily increases. No restoration of brain metabolism was observed when the oxygen-poisoned tissue was returned to normal pressure nor could it be restored by any of the methods tried. From the data, it was concluded that if the oxygen poisoning of brain respiration is responsible for the convulsion produced by oxygen at high pres-

sure, the clinical effects must occur when only a small percentage of brain respiration has been poisoned by oxygen. The order of sensitivity to oxygen of the respiration of various rat tissues was given in the following diminishing sequence: cerebral cortex, spinal cord, liver, testis, kidney, lung, and muscle. In addition to poisoning the oxidation of glucose, oxygen also was found to poison the capacity of the brain tissue to oxidize fructose, lactate, and pyruvate. The capacity of the brain slices to oxidize succinate is much less affected than for the other substrates. Feeding the rats a diet rich or poor in the B-factors had no significant effect upon brain metabolism. It was suggested that oxygen may poison primarily the pyruvate oxidase system, probably attacking the essential SH group of the enzyme. Attention was drawn to a parallelism between the action of narcotics and of oxygen on cell metabolism. Both interfere with pyruvate oxidation, but they may act upon different links in the enzyme complex. For a further study on the toxic effects of oxygen on tissue enzymes, a paper by Dickens (*2298*) 1946 should be consulted.

For further investigations of the metabolic changes produced by oxygen poisoning, papers by the following should be consulted: Stadie, Riggs, and Haugaard (*2302, 2303*) 1945, and Stadie and Haugaard (*2301*) 1946. Stadie, Riggs, and Haugaard (*2302*) determined metabolic activity in vitro of surviving tissues exposed to high oxygen pressures in comparison with similar tissues under 1 atmosphere of oxygen. Thin slices of brain from animals killed by high-pressure oxygen showed no significant change in total oxygen uptake or respiratory quotient when these were subsequently determined by the Warburg technique at 1 atmosphere of oxygen. Similar preparations of brain slices and homogenates from normal animals exposed in a preliminary period to high oxygen pressures and subsequently observed in a Warburg apparatus at 1 atmosphere of oxygen showed a steadily decreasing rate of oxygen uptake in proportion to the pressure of oxygen and the time of exposure. Inhibition of brain metabolism by high oxygen pressures was similar with glucose, fructose, pyruvate, or lactate as the substrate. Similar results were obtained when normal tissues was observed at 8 atmospheres of oxygen. The initial rate of oxygen uptake was halved in approximately 1 hour's time. The time required for appreciable reduction in the rate of oxygen uptake was found to be far greater than for the production of serious symptoms, convulsions, and deaths when intact animals were subject to the same oxygen pressure. Brain slices subjected to relatively high pressures of carbon dioxide (up to 107 mm. Hg) in addition to 8 atmospheres of oxygen were no more susceptible to oxygen poisoning than those exposed to 8 atmospheres of oxygen alone. The metabolism of brain in vitro, although diminished, was not altered from its predominantly carbohydrate character by high oxygen pressure. Attempts to reverse lowered oxygen uptake of poisoned brain tissue by early return to 1 atmosphere failed. The rate of oxygen uptake of brain tissue in vitro at 1 atmosphere of oxygen was not affected by 7 additional atmospheres of nitrogen or helium. On the basis of these experiments, the author concluded that generalized tissue anoxia is not the cause of acute oxygen poisoning. Alternative hypotheses are discussed.

Stadie, Riggs, and Haugaard (*2303*) 1945 have investigated the effects of high oxygen pressures upon the metabolism of liver, kidney, lung, and muscle tissue. Regarding the liver, they found that at high pressures of oxygen, the rate of oxygen uptake during the first hour in the case of isolated tissue did not differ significantly from that at 1 atmosphere. As in the case of brain tissue, the rate of oxygen uptake in liver tissue fell slowly and steadily during exposure, but the rate reached 50 percent of the control rate only after 3½ hours as opposed to 1 hour in the case of brain. As with brain tissue, although there is a definite effect of high oxygen pressure on oxygen uptake of liver slices, the extent of the effect is negligible until long after the time required to distinguish the last signs of life in intact animals under similar conditions. In experiments on kidney slices, it was found that long preliminary exposures were required to reduce the oxygen uptake significantly. The sensitivity of the kidney slices to high oxygen pressure lies midway between that of brain and liver slices. Again it was seen that the falling off in respiration takes place long after an intact animal would have succumbed. The mean respiratory quotient was not significantly different from that observed at 1 atmosphere. Oxygen uptake of rat diaphragm was measured during exposure of isolated tissue to 8 atmospheres of oxygen. This muscle was found to be more resistant to oxygen poisoning than all other tissues examined. The initial rate under high oxygen pressure was not significantly different from that under 1 atmosphere, and fell off very slowly. The authors conclude that the slow development of loss of metabolic activity indicates that this plays little or no role in the acute phase of oxygen poisoning or early death of intact experimental animals. Stadie and Haugaard (*2301*) 1946 showed that intact animals under 8 atmospheres of oxygen rapidly developed

severe symptoms of oxygen poisoning without showing decreases of oxygen consumption.

Riggs (*2300*) 1945 found that the tone of the pyloric sphincter muscle of rabbits is depressed by exposure to oxygen under high pressure at a rate similar to that at which the intact animal succumbs under similar conditions to convulsions and death. The total oxygen uptake of the muscle was found to be not significantly affected by high oxygen pressure during the time at which its tone was depressed.

According to Bean (*2296*) 1951, repeated short exposure of baby albino rats to oxygen at high pressure interferes with normal growth. This and the recognition that conditions of stress alter adrenal cortical activity suggested that exposure to oxygen at high pressure might also induce gross and microscopic changes in the adrenals. Experiments were therefore carried out in which each of several litters of baby and young adult rats were divided into test and control groups. The test animals were exposed to oxygen at about 70 lbs. gage pressure for several minutes, followed by a long interval of rest, 4 times a day over periods from 2 weeks to 3 months. The adrenal glands of the test animals exposed over the longer periods followed by 7 months of nonexposure were significantly larger and heavier than adrenals of control animals. The adrenal glands of animals killed immediately following the termination of the shorter exposure schedules were also distinctly larger and heavier than their controls. Gersh and Wagner (*2299*) 1944 found in cats that hypothyroidism lengthened the time of onset of the convulsive seizures and decreased the cumulative neurological damage. Conversely, hyperthyroidism was found to increase the sensitivity of the animals to oxygen at high pressure.

For further studies on metabolic changes in oxygen poisoning, papers by Van Goor and Jongbloed (*2304*) and (*2305*) 1949, and (*2306*) 1950 may be consulted.

2296. Bean, J. W. Adrenal alteration induced by oxygen at high pressure. *Fed. Proc. Amer. Soc. exp. Biol.,* 1951, *10:* 11.

2297. Dickens, F. The toxic effects of oxygen on brain metabolism and on tissue enzymes. 1. Brain metabolism. *Biochem, J.,* 1946, *40:* 145–171. Gt. Brit. MRC–RNPRC, UPS. *R. N. P. 44/146, U. P. S. 51,* March 1944, 80 pp. [P]

2298. Dickens, F. The toxic effects of oxygen on brain metabolism and on tissue enzymes. 2. Tissue enzymes. *Biochem. J.,* 1946, *40:* 171–187. [P]

2299. Gersh, I. and C. E. Wagner. Metabolic factors in oxygen poisoning. U. S. Navy. NMRI. *Project X–192, Rept. no. 3,* 30 October 1944, 8 pp. [P]

2300. Riggs, B. C. The effect of exposure to oxygen at high pressure upon the tonus and respiration of pyloric muscle from the rabbit. *Amer. J. Physiol.,* 1945, *145:* 211–217. [P]

2301. Stadie, W. C. and N. Haugaard. Oxygen poisoning. X. The effect of oxygen at eight atmospheres upon the oxygen consumption of the intact mouse. *J. biol. Chem.,* 1946, *164:* 257–263. [P]

2302. Stadie, W. C., B. C. Riggs, and N. Haugaard. Oxygen poisoning. III. The effect of high oxygen pressures upon the metabolism of brain. *J. biol. Chem.,* 1945, *160:* 191–208. [P]

2303. Stadie, W. C., B. C. Riggs, and N. Haugaard. Oxygen poisoning. IV. The effect of high oxygen pressures upon the metabolism of liver, kidney, lung, and muscle tissue. *J. biol. Chem.,* 1945, *160:* 209–216.

2304. Van Goor, H. and J. Jongbloed. Oxygen poisoning. *Enzymologia,* 1949, *13:* 313–324. [P]

2305. Van Goor, H. and J. Jongbloed. Zuurstofvergiftiging in vitro en in vivo. *Ned. Tijdschr. Geneesk.,* 1949, *93:* 2118–2120.

2306. Van Goor, H. and J. Jongbloed. Oxygen poisoning in vitro and in vivo. *Acta brev. neerl. Physiol.,* 1950, *17:* 49–52. [P]

C. MECHANISMS OF INTOXICATION

1. ROLE OF CARBON DIOXIDE AND OTHER FACTORS IN OXYGEN INTOXICATION

A discussion of the literature on the mechanism of the poisonous action of oxygen is found on pages 193 and 194 of the first volume of this Sourcebook. We have also discussed the problem in the present volume under general studies in the section on the effects of oxygen tension in excess of 1 atmosphere (p. 187). Reference is made there to recent papers by Lambertsen and coworkers who have indicated that the cause of convulsions remains uncertain, but that at present the explanation appears to rest upon one or more of the following: (1) a direct toxic effect of high oxygen pressures upon certain constituents of brain cells, (2) an accumulation of carbon dioxide in toxic amounts in the central nervous system due to the breakdown in normal transport function of hemoglobin for this gas, and (*3*) changes in cerebral circulation. Too late for inclusion in the bibliographical lists of the present volume is a report by Lambertsen and his colleagues in the Journal of Applied Physiology, Volume V, No. 10, 1953, on the role of carbon dioxide.

A number of workers have reported accumulation of carbon dioxide in oxygen poisoning. Campbell and Poulton (*2307*) 1938 stated that an effect of oxygen breathing is to increase the carbon dioxide content of tissues; they suggested that convulsions are due in some measure to a great increase of carbon dioxide pressure in the tissues. Pichotka (*2313*) 1946 subjected guinea pigs and rabbits to oxygen tensions ranging from 3.5 to 5.8 atmospheres. The author believed that oxygen poisoning is due to carbon dioxide accumulation in the periphery. During acute oxygen poisoning, the oxygen tension of

the tissues reached 300 mm. Hg and the carbon dioxide tension reached 200 mm. Hg. When animals were exposed to 20 to 35 percent carbon dioxide in a normal oxygen atmosphere, it was found that the histological picture in the lung and liver were the same as in oxygen poisoning, although the clinical picture was different. The author considered that oxygen poisoning is an indirect carbon dioxide poisoning.

Seelkopf and von Werz (*2314*) 1948 also found an accumulation of carbon dioxide in the tissue in oxygen poisoning in guinea pigs exposed to oxygen under pressure. This carbon dioxide congestion was considered mainly due to the delay of carbon dioxide pickup and transport. Taylor (*2316* and *2317*) 1949 placed cats in a glass chamber in which they breathed oxygen at atmospheric pressure. Breathing oxygen at atmospheric pressure led to convulsions and there was a progressive fall in tissue oxygen tension and a progressive rise in tissue carbon dioxide tension until death or convulsions occurred. The tissue oxygen tension of cats exposed intermittently to oxygen and air at atmospheric pressures showed a fall and then a rise to a consistent value, this being somewhat less than the original normal value when the animal was breathing air. The tissue carbon dioxide tension showed little change. Animals thus treated were acclimatized to subsequent continuous oxygen exposure. This effect was not permanent, but was still present 7 weeks after acclimatization. When the cats convulsed, the tissue oxygen tension was near the value for normal cats breathing air. Convulsions were considered by the author to be due neither to increased oxygen tension in the tissues nor to anoxia. Since the carbon dioxide tissue gas tensions were much higher than normal, this was believed to support the view that one factor in the production of convulsions is the accumulation of carbon dioxide in the tissues. In a subsequent paper published in 1949, Taylor (*2317*) found in cats breathing oxygen at high pressure that both the oxygen and the carbon dioxide tissue tensions reached high values. Additional carbon dioxide shortened the time required for the onset of oxygen convulsions. This effect was most striking in cats whose convulsion time in oxygen without added carbon dioxide is comparatively long.

Stroud, Lambertsen, Kough, Gould, and Ewing (*2315*) 1951, in a study of the effect of oxygen inhalation at increased ambient pressures upon tissue carbon dioxide tension in small animals and psychotic patients, were not able to find a marked immediate rise of subcutaneous carbon dioxide tension. The rises observed were slow in onset and accompanied by pulmonary damage and respiratory failure in the small animals. No appreciable increase of "tissue" carbon dioxide tension occurred in human subjects prior to the onset of oxygen convulsions. The rapid rise of carbon dioxide tension found by previous workers is considered by the authors to be probably not due to the loss of the dual function of hemoglobin, but appears to be the result of other factors such as (1) pulmonary damage by oxygen and by decompression, (2) respiratory depression, and (3) diffusion of carbon dioxide into the depot during decompression of the animal for gas sampling. In the authors' experiments, gas sampling was performed at the pressure of exposure to oxygen.

Kough, Lambertsen, Stroud, Gould, and Ewing (*2312*) 1951 carried out four types of experiments using human subjects at 3½ atmospheres of inspired oxygen in an attempt to evaluate the role of carbon dioxide in acute oxygen toxicity. In four men carried to convulsions, the highest carbon dioxide tension in subcutaneous gas depots was 50 mm. Hg. In 12 subjects, the internal jugular carbon dioxide tension increased 3 mm. Hg, while the arterial carbon dioxide tension decreased 5 mm. Hg. In seven subjects, cerebral blood flow decreased 25 percent. Cerebral vascular resistance increased 50 percent, while the cerebral oxygen consumption was unchanged so that the internal jugular oxygen tension was only 75 mm. Hg. In man, it appears, therefore, that any elevation of tissue carbon dioxide tension accompanying acute oxygen poisoning at 3½ atmospheres is adequately explained by loss of the dual function of hemoglobin and changes in blood flow, and that elevation of tissue carbon dioxide tension is not sufficient per se to produce convulsions. The significant finding in 7 experiments on 4 subjects who breathed 2 percent carbon dioxide in oxygen at 3½ atmospheres was a decrease in the cerebral arteriovenous oxygen difference resulting in an increase in the internal jugular oxygen tension to a mean value of 800 mm. Hg. One way that the breathing of carbon dioxide may conceivably hasten the onset of oxygen convulsions is by increasing the cerebral blood flow so that a larger bulk of the brain is exposed to higher and presumably more toxic levels of oxygen.

2307. Campbell, A. and E. P. Poulton. Oxygen poisoning. pp. 42–45 in: *Oxygen and carbon dioxide therapy.* Oxford University Press, London, Humphrey Milford, 1938, 202 pp. [R]

2308. Cass, R. E. Effects of high oxygen tensions upon the carbon dioxide production of skeletal muscle and other tissues of the frog. *Amer. J. Physiol.*, 1947, *148:* 490–506. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 495. Abstr. [P]

2309. Haldane, J. B. S. Oxygen poisoning in man. *Brit. Med. J.*, 1947, *2:* 226.

2310. Hill, L. Oxygen poisoning in man. *Brit. Med. J.*, 1947, *2:* 396.

2311. Kough, R. H., C. J. Lambertsen, M. W. Stroud, R. A. Gould, and J. H. Ewing. Some observations on the role of carbon dioxide in acute oxygen toxicity at 3½ atmospheres inspired oxygen tension. *Amer. J. med. Sci.*, 1951, *221:* 354.

2312. Kough, R. H., C. J. Lambertsen, M. W. Stroud, R. A. Gould, and J. H. Ewing. Role of carbon dioxide in acute oxygen toxicity at 3½ atmospheres inspired oxygen tension. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 76.

2313. Pichotka, J. Experimentelle Untersuchungen zur Ursache der Sauerstoff-Vergiftung. (lecture translation). U. S. AAF. Aero medical center, HQ. 3D. Central medical establishment. *D2–46–35*, 28 February 1946, 9 pp. [P] [R]

2314. Seelkopf, K. and R. von Werz. Über die Rolle der Kohlensäure bei der Sauerstoffvergiftung. *Arch. exp. Path. Pharmak.*, 1948, *205:* 351–366. [P]

2315. Stroud, M. W., C. J. Lambertsen, R. H. Kough, R. A. Gould, and J. H. Ewing. Effect of oxygen inhalation at increased ambient pressures upon tissue carbon dioxide tension. *Fed. Proc. Amer. Soc. exp. Biol.*, 1951, *10:* 338.

2316. Taylor, H. J. The effect of breathing oxygen at atmospheric pressure on tissue oxygen and carbon dioxide tensions. *J. Physiol.*, 1949, *108:* 264–269. [P]

2317. Taylor, H. J. The role of carbon dioxide in oxygen poisoning. *J. Physiol.*, 1949, *109:* 272–280. [P]

2. DISTURBANCES OF CELLULAR METABOLISM IN THE PRODUCTION OF OXYGEN INTOXICATION

For studies on the effects of oxygen at high pressure on metabolism, the reader is referred to appropriate sections on pages 192 and 193. Many experimental findings support the theory that oxygen poisoning is the result of interference with cellular metabolism. Factors which increase aerobic metabolic requirements decrease the time of onset of oxygen seizures, and those which decrease the metabolic rate prolong the time of onset. Gersh and Wagner (*2319*) 1945 found that hyperthyroidism produced in animals by oral administration of thyroid decreased the time of onset of convulsions. Thyroidectomy increased the time of onset of seizures due to breathing oxygen at high pressure in cats. Administration of thiourea or thiouracil could not be shown to have an effect, and in these experiments no histological evidences of thyroid inhibition were seen. Changes in environmental temperature (within the range between 22° C. and 41° C.) had no effect on oxygen seizures, whereas either elevation or depression of body temperature increased the susceptibility of the cat to seizures. Administration of oxygen under pressure (105 lbs. gage pressure) did not cause marked fall in temperature. Young cats were found to be more resistant to oxygen seizure than older ones, and the authors suggested that the greater reliance of the young brains on anaerobic metabolism is the explanation of this finding. A significant correlation between thyroid activity and susceptibility to the poisonous action of oxygen at high pressure has been determined by Grossman and Penrod (*2321*) 1949. Seventy-five rats of approximately 200 grams each were divided equally into three groups. All were fed a stock diet to which was added propyl-thiouracil for 22 days for one group and desiccated thyroid powder for 8 days for the second group. The third group served as controls. Oxygen consumption was determined at 1-atmosphere pressure, after which all the animals were exposed to 5.5 atmospheres of oxygen for 1 hour. There was a highly significant inverse correlation between oxygen consumption and survival rate in the three groups. In the hypothyroid rats, 80 percent of the animals survived. In the control group, there was a 56-percent survival. In the hyperthyroid group, there was a survival of 29 percent of the animals. The authors suggested that carbon dioxide production and accumulation is an important factor in the etiology of high oxygen poisoning. Five and one-half atmospheres of oxygen for 1 hour is considered to be the approximate LD_{50} for the strain and age of rats used.

In a study of the relation between inactivation of enzymes by oxygen and essential sulfhydryl groups, Haugaard (*2322*) 1946 reported that some sulfhydryl enzymes while stable in the presence of air are inactivated by oxygen at high pressure. Succinic dehydrogenase is inactivated by 2 to 4 hours of exposure to oxygen at 7 atmospheres. Lactic acid dehydrogenase is rapidly inactivated at 38° C. at 7 atmospheres in air or oxygen. At 26° C. there was no appreciable inactivation. Exposure to 7 atmospheres of oxygen for 4 hours at 38° C. did not affect acid phosphatase activity of rat-kidney homogenate. Phosphorylation of glucose (rabbit-kidney extract) was unaffected by high-pressure oxygen. Enzyme reactions inhibited by exposure to 7 atmospheres of oxygen at 38° C. were malic dehydrogenase, pyruvic oxidase, choline dehydrogenase, glutamic acid dehydrogenase, and alpha-keto-glutaric oxidase (all rat tissue). Only one of the enzymes studied contained the sulfhydryl group—cholinesterase—was resistant to the action of oxygen at high pressure. The toxic action of oxygen is slow in intact tissue, making it difficult to correlate enzyme inhibition with the rapid onset of symptoms exhibited in intact rats exposed to oxygen at high pressure.

Lenggenhager (*2323*) 1950 found that animals exposed to 3 to 6 atmospheres of oxygen die within a few hours. The idea that accumulation of tissue carbon dioxide is the cause of high oxygen death was rejected by this author. He based his con-

clusion in part on the finding of normal carbon dioxide values in the cerebrospinal fluid of 2 human subjects exposed to 3 atmospheres of pure oxygen for 30 minutes. The clinical picture preceding oxygen death points to a predominantly cerebral cause. However, no histological alterations could be traced in the brains of animals killed by oxygen. Injection of a redox indicator revealed that the reducing power of an excised brain can be markedly lowered by storing the brain under high pressure of oxygen. However, when the dye was injected into the brain of an animal freshly killed by oxygen, the method failed to demonstrate an abnormally low reducing power. It was argued by the author that oxygen death must be brought about by changes in redox potentials too small to be detected by present techniques, yet sufficient to impair cerebral function.

For further studies on metabolic factors in the production of oxygen intoxication, papers by Allen and Mortarotti (*2318*) 1948 and White (*2324*) 1945 may be consulted.

2318. Allen, S. C. and T. G. Mortarotti. The effect of rutin on oxygen toxicity in rats. *Fed. Proc. Amer. Soc. exp. Biol.*, 1948, *7:* 202. [P]

2319. Gersh, I. and C. E. Wagner. Metabolic factors in oxygen poisoning. *Amer. J. Physiol.*, 1945, *144:* 270–277. *J. industr. Hyg.*, 1946, *28:* abstract section: 13. [P]

2320. Grossman, M. S. and K. E. Penrod. Relationship of hypothermia to high oxygen poisoning. *Amer. J. Physiol.*, 1949, *156:* 177–181. [P]

2321. Grossman, M. S. and K. E. Penrod. The thyroid and high oxygen poisoning in rats. *Amer. J. Physiol.*, 1949, *156:* 182–184. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 321. [P]

2322. Haugaard, N. Oxygen poisoning. XI. The relation between inactivation of enzymes by oxygen and essential sulfhydryl groups. *J. biol. Chem.*, 1946, *164:* 265–270. [P]

2322. Lenggenhager, K. Warum wirkt Sauerstoffüberdruck rasch tödlich? *Z. ges. exp. Med.*, 1950, *116:* 353–377. [P]

2324. White, W. A. Oxygen poisoning in man, effect of cysteine hydrochloride and ammonium chloride on the time of onset of toxic symptoms. U. S. Navy. NMRI. *Project X–435, Rept. no. 1,* 13 August 1945, 3 pp.

D. EFFECT OF HIGH OXYGEN TENSIONS ON MICRO-ORGANISMS

The older literature (see p. 189 of the first volume of this Sourcebook) indicates that oxygen under high pressure inhibits or deleteriously affects the activity of certain micro-organisms. A more recent study by Porter and Bean (*2325*) 1946 may be consulted for a report of the adverse influence of increased oxygen pressure on malarial parasites in vitro and in vivo. In these studies, the parasite *Plasmodium lophurae* was used. The viability of these parasites in duck or chick bloods exposed to oxygen at various pressures was compared with that in control bloods kept under room conditions. Exposure to oxygen for 6 hours at 30 to 60 lbs. gage pressure reduced the parasite viability to 68 percent or more below that of controls. Six hours of exposure at 15 lbs. gage pressure did not lower viability appreciably. Exposure to oxygen for 12 hours at 15 lbs. gage pressure gave moderate reduction of viability, but no reduction at atmospheric pressure. Previous in vivo studies revealed no detectable effect on the proportion of parasitized erythrocytes in infected chicks given repeated short exposures to oxygen at 50 and 90 lbs. gage pressure. Because of the toxicity of these pressures, the authors utilized pressures below 15 lbs. gage pressure. Infected chicks were kept 5 or 6 days in oxygen at atmospheric pressure or at 300 to 500 mm. Hg gage pressure for about 10 hours a day. At the peak of infection, the proportion of parasitized erythrocytes in test chicks was 64 to 86 percent lower than in controls. The data indicate that increased oxygen pressure enhances the destruction of *Plasmodium lophurae* in drawn blood, and suppresses parasitemia in infected birds.

2325. Porter, R. J. and J. W. Bean. Adverse influence of increased oxygen pressure on malarial parasites in vitro and in vivo. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 82.

E. OXYGEN PARADOX

Under certain circumstances rapid recompression to sea level from simulated high altitudes or administration of oxygen following a period of hypoxia results in untoward psychological, cardiovascular, and neuromotor symptoms. There may be mental confusion, cardiovascular collapse, and muscular incoordination or convulsions. These effects are spoken of as the oxygen paradox.

A thesis by Bouverot (*2326*) 1949 reviews completely the subject of the oxygen paradox. Dogs given oxygen following hypoxia showed a slowing of the respiratory rate, reduction of cardiac rate, and a drop in arterial blood pressure. An incoordination of movements was also observed. Sometimes convulsions occurred, these being either clonic or tonic. In man, there were psychic disturbances including euphoria and defects of judgment.

A description of the paradoxic response following oxygen administration in patients with chronic anoxemia is given by Comroe, Bahnson, and Coates (*2327*) 1950. Psychic changes were noted in 8 of 65 patients. No patient became somnolent unless (*a*) the initial arterial pCo_2 was 50 mm. Hg. or more, (*b*) the arterial oxygen saturation was below 90 percent, and (*c*) oxygen therapy relieved the anox-

emia. The authors believe that the mechanism for the paradoxic response may possibly involve carbon dioxide narcosis, cerebral vasospasm, reflex depression, increased cerebrospinal fluid pressure, or direct depression of the cerebral cortex by high oxygen tensions.

For experimental studies on paradoxic effects of oxygen in human hypoxia, the reader is referred to papers by Latham (*2333*) 1948 and (*2334*) 1951. Sixty exposures of 52 people at 20,000 feet simulated altitude were made; 13 of these manifested paradoxic symptoms during oxygen administration. Writing-test errors reached a peak 12 seconds after oxygen inhalation. Cardiovascular responses followed approximately 40 seconds later, and these were accompanied by musuclar incoordination and mental confusion. Later, there was threat of cardiovascular collapse associated with a fall in blood pressure and an increase in peripheral flow.

Lemaire, Franck, and Grandpierre (*2335*) 1950 recorded electroencephalograms of nonanesthetized subjects during a 3-minute exposure to 7-percent oxygen in nitrogen followed by oxygen inhalation. During the experiment the subjects were kept in a dark and silent room with their eyes closed and were ignorant of the actual changes in the respiratory air. During the anoximic phase, the usual decrease in the frequency of the electroencephalographic waves was observed. After the inhalation of pure oxygen a phase of "electrical silence" appeared, flattening of the waves starting after 3 or 4 respirations in pure oxygen and lasting from 15 to 20 seconds. Following this, the EEG pattern returned to that manifested at the beginning of the experiment.

According to Grandpierre, Franck, and Lemaire (*2329, 2330*) 1948, there is a depression of the respiratory center in chloralosed dogs given 100-percent oxygen after a brief period of anoxemia.

For other general reports on the oxygen paradox, the reader may consult articles by Franck, Grandpierre, and Royer (*2328*) 1948; Grandpierre, Franck, and Lemaire (*2331*) 1948 and (*2332*) 1950; Malmejac, Chardon, and Neverre (*2336*) 1947 and (*2337*) 1949; and U. S. Army (*2338*) 1945.

2326. Bouverot, P. Contribution à l'étude de l'action paradoxale de l'oxygène. Thèse. (Méd.) Paris, Lyon, 1949, 144 pp.

2327. Comroe, J. H., Jr., E. R. Bahnson, and E. O. Coates, Jr. Mental changes occurring in chronically anoxemic patients during oxygen therapy. *J. Amer. med. Ass.,* 1950, *143:* 1044–1048. [CH]

2328. Franck, C., R. Grandpierre, and P. Royer. Apnée provoquée chez l'homme par inhalation d'un mélange gazeux riche en oxygène au cours de l'anoxémie. *C. R. Soc. Biol., Paris,* 1948, *142:* 376–378. [P]

2329. Grandpierre, R., C. Franck, and R. Lemaire. L'excitabilité du centre réspiratoire dans l'action paradoxale de l'oxygène. *C. R. Soc. Biol., Paris,* 1948, *142:* 1028–1029. [P]

2330. Grandpierre, R., C. Franck, and R. Lemaire. Les modifications du rythme cardiaque dans l'action paradoxale de l'oxygène. *C. R. Soc. Biol., Paris,* 1948, *142:* 1030–1031. [P]

2331. Grandpierre, R., C. Franck, and R. Lemaire. L'action paradoxale de l'oxygène. Son intérêt en médecine aéronautique. *Méd. aéronaut.,* 1948, *3:* 199–226. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1949, *2:* 641. Abstr. [R]

2332. Grandpierre, R., C. Franck, and R. Lemaire. Travaux originaux-l'action paradoxale de l'oxygène. *J. Physiol., Paris,* 1950, *42:* 5–30. [R] [P]

2333. Latham, F. Studies on the oxygen paradox. Gt. Brit. FPRC. Institute of aviation medicine, Farnborough. *F. P. R. C. rept. no. 705,* December 1948, 10 pp.

2334. Latham, F. The oxygen paradox. Experiments on the effects of oxygen in human anoxia. *Lancet,* 1951, *1:* 77–81. [P]

2335. Lemaire, R., C. Franck, and R. Grandpierre. Les modifications de l'activité électrique du cerveau dans l'action paradoxale de l'oxygène chez l'homme. *C. R. Soc. Biol., Paris,* 1949, *143:* 1111–1112. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1098.

2336. Malmejac, J., G. Chardon, and G. Neverre. Action paradoxale de l'oxygène sur les centres vasomoteurs. *C. R. Soc. Biol., Paris,* 1947, *141:* 396–398. [R]

2337. Malmejac, J., G. Chardon, and G. Neverre. Rôle éventuel de l'influence excitante directe du déficit en oxygène sur les centres vaso-moteurs dans la production de l'action paradoxale de l'oxygène. *C. R. Soc. Biol.,* Paris, 1949, *143:* 694–696. [P]

2338. U. S. Army. Combined intelligence objectives subcommittee. Part I. Aviation medicine. pp. 4–19 in: *Aviation medicine, general medicine, veterinary medicine, and chemical warfare. C. I. O. S. Target nos. 24/17 and 25/82,* 27 April 1945, 48 pp.

VI. NOXIOUS AGENTS

A. GENERAL STUDIES OF NOXIOUS AGENTS

Du Bois has carried out pioneer research on noxious gases and other agents occurring in submarines. A classical paper on this subject by Du Bois (*2340*) 1919 should be read. The reader is also recommended to examine the standard texts and monographs on toxicology. Reference is made to the monograph by Elkins (*2341*) 1950 for up-to-date discussions of industrial toxic hazards, organic and inorganic compounds, prevention methods, maximal allowable concentrations of toxic agents, sampling and measuring devices, and analytical methods and procedures. Maximum allowable concentrations of atmospheric contaminants have also been listed by Cook (*2339*) 1945.

2339. Cook, W. A. Maximum allowable concentrations of industrial atmospheric contaminants. *Industr. Med.,* 1945, *14:* 936–946.

2340. **Du Bois, E. F.** Gases occurring in submarines. pp. 9–19 in: Review of recent work on air purification in submarines. U. S. Navy. BuMed. *Submarine ventilation. Bulletin No. 4* (*126632*), March 15, 1919, 47 pp.

2341. **Elkins, H. B.** *The chemistry of industrial toxicology.* New York, John Wiley & Sons, Inc., 1950, ix, 406 pp. [R]

B. NOXIOUS GASES, DUSTS, AND VAPORS

1. CARBON MONOXIDE

(a) General Studies of Carbon Monoxide Poisoning

New problems of possible carbon monoxide hazards are posed by the development of snorkeling. With strong following winds, engine exhaust gases may not be carried away completely from the air intake. Leaks in the exhaust lines within the submarines may also give rise to carbon monoxide poisoning. In deep-sea diving, faulty compressors may carry down carbon monoxide to the diver himself. A similar problem may exist in caisson operations. A further carbon monoxide hazard arises in connection with regeneration of the air in submarines. Chemical generation of oxygen by means of the chlorate candle may introduce some carbon monoxide into the air. Concentrations of carbon monoxide in the air become more hazardous in proportion to reduction of the partial pressure of oxygen or increased atmospheric pressure as in deep-sea diving.

Although there is a considerable bulk of literature on carbon monoxide poisoning, knowledge of the actual mechanism of carbon monoxide intoxication has not advanced far beyond that reported in the first volume of this Sourcebook. Among the general references that follow, papers by the following are particularly significant: Campbell and Fulton (*2342*) 1938, Gt. Brit. Factory Department, Ministry of Labour and National Service (*2350*) 1945, Hamilton and Hardy (*2351*) 1949, Jacobs (*2352*) 1949, McConnell (*2354*) 1951, Reed and Harcourt (*2358*) 1941, Rossiter (*2359*) 1947, and Sayers (*2360*) 1951.

2342. **Campbell, A. and E. P. Poulton.** Carbon monoxide poisoning, etc. pp. 113–119 in: *Oxygen and carbon dioxide therapy.* London, Oxford University Press, 1938, 202 pp.

2343. **Dahlström, H., G. Obreschkow, and T. Sjöstrand.** A comparison between the effects of carbon monoxide poisoning and inhalation of air with low oxygen content upon respiration, circulation, alkaline reserve of the plasma and patellar reflex in normal subjects and in cases of "Chronic Producer Gas Poisoning." *Acta pharm. toxicol., Kbh.*, 1947, *3:* 105–123. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1948, *1:* 693. Abstr. [P]

2344. **Flandin, C. and J. Guillemin.** *L'intoxication oxycarbonée.* (*Étude clinique et thérapeutique*). Paris, Masson et Cie, 1942, 156 pp. [R]

2345. **Forssman, S., B. Gullberg, and A. Svensson.** Gengasförgiftnings problemen. *Nord. Med., Stockholm,* 1946, *32:* 2716–2722. [P]

2346. **Fourcade, J.** Intoxications par l'oxyde de carbone. pp. 172–196 in: *Médecine du travail.* Edited by C. Simonin. Paris, Librairie Maloine, 1950, 913 pp. [D]

2347. **Fridliand, I. G.** K pathogenezy otravlenii okis'iu ugleroda v Leningrade v 1941–1943 gg. [Pathogenesis of carbon monoxide poisoning in Leningrad in 1941–1943.] pp. 65–88 in: *Otravleniia okis'iu ugleroda v osazhdennom Leningrade v 1941–1943 gg.* [Carbon monoxide poisoning in besieged Leningrad in 1941–1943.] Leningrad, S. M. Korova, 1947, 118 pp.

2348. **Fridliand, I. G.** Nekotorye osobennosti kliniki intoksikatsii okis'iu ugleroda v Leningrade v 1941–1943 gg. [Certain characteristics in the clinical aspects of carbon monoxide poisoning in Leningrad, 1941–1943.] *Sovetsk. Vrach. Zh.*, 1947, *5:* 13–17.

2349. **Fridliand, I. G.** Nekocorye voprosy terapii. [Therapeutic problems.] pp. 93–106 in: *Otravleniia okis'iu ugleroda v oxazhdennom Leningrade v 1941–1943 gg.* [Carbon monoxide poisoning in the besieged Leningrad in 1941–1943.] Leningrad, S. M. Kirova, 1947, 118 pp.

2350. **Gt. Brit., Factory department, Ministry of labour and national service.** Memorandum on carbon monoxide poisoning. *Form 827,* May 1945, 32 pp.

2351. **Hamilton, A. H. and H. L. Hardy.** Asphyxiants. pp. 219–267 in: *Industrial toxicology.* New York, Paul B. Hoeber, Inc., 1949.

2352. **Jacobs, M. B.** Carbon monoxide, carbon dioxide, cyanides, and nitriles. pp. 401–466 in: *The analytical chemistry of industrial poisons, hazards, and solvents.* New York, Interscience Publishers, Inc., 1949, 788 pp.

2353. **Kohn-Abrest, M.** Sur l'oxycarbonémie. *Arch. mal. Prof.*, 1949, *10:* 37–38. [D]

2354. **McConnell, W. J.** Diseases due to chemical agents. Carbon monoxide poisoning. pp. 507–508 in: *A textbook of medicine.* Edited by R. L. Cecil and R. F. Loeb. Philadelphia, W. B. Saunders Co., 1951, 1549 pp.

2355. **Moeschlin, S.** Zum Problem der Kohlenoxydvengiftung (Leuchtgas). *Schweiz. med. Wschr.*, 1946, *76:* 508–510. Abstr. [R]

2356. **Pierquin, L.** Acquisitions récentes concernant l'intoxication oxycarbonée professionnelle. *Méd. usine,* 1950, *12:* 101–102. [D]

2357. **Raymond, V. and A. Vallaud.** *L'oxyde de carbone et l'oxycarbonisme.* Institut national de sécurité pour la prévention des accidents du travail et des maladies professionnelles, Paris, 1948, 367 pp.

2358. **Reed, J. V., and A. K. Harcourt.** Carbon monoxide pp. 24–31 in: *The essentials of occupational diseases.* Springfield, Charles C. Thomas, 1941, 225 pp.

2259. **Rossiter, F. S.** Carbon monoxide. pp. 113–129 in: *Introduction to industrial medicine.* Edited by T. Lyle Hazlett. Second edition. Chicago, Industrial Medicine Publishing Co., 1947, 260 pp.

2360. **Sayers, R. R.** Carbon monoxide poisoning. pp. 123–129 in: *Practice of medicine.* Volume 8. Edited by Frederick Tice. Hagerstown, W. F. Prior Co., Inc., 1951, 627 pp.

2361. **Wohlfart, G., B. Gullberg, and A. Svensson.** Differential diagnostiska synpunkter på akut och kronisk koloxidförgiftning. *Nord. Med., Stockholm,* 1946, *32:* 2726–2734.

2362. **Zahle, V.** Om den akute kulilteforgiftning. *Ugeskr. Laeg.*, 1948, *110:* 1024.

2363. Anon. Case 37. Carbon monoxide poisoning. *Amer. Practit.*, 1947/48, *2:* 411–414.

(b) Carbon Monoxide in Submarines and Other Naval Vessels

Although there are a variety of carbon monoxide problems on board submarines, experience has shown that carbon monoxide poisoning rarely occurred in normal submarine operations prior to the use of the snorkel. In normally functioning submarines in the presnorkel period, practically no carbon monoxide was forced into the boat. Malorny, in 1948 (*2365*), reporting on carbon monoxide in submarines in the German submarine fleet during World War II, stated that the content of carbon monoxide in diesel exhaust gases was rather low. Malorny reported that during normal snorkel operations, concentrations of carbon monoxide of 0.01 up to 0.04 volume percent developed. The crew was exposed to such concentrations for many hours without interruption. During submerged operations with the snorkel there was an increase of negative pressure within the boat if a wave broke over the snorkel head or if an inexperienced planesman did not maintain correct snorkel depth. Under such circumstances reduction of oxygen partial pressure resulted in increased toxicity of the carbon monoxide, especially in the engineroom. In submerged snorkel operations the carbon monoxide concentration in the engineroom sometimes attained toxic values from 0.10 to 0.24 volumes percent of carbon monoxide. Many cases of central nervous system damage occurred as a sequel to carbon monoxide poisoning, and it is known that there were deaths attributed to carbon monoxide poisoning in the German submarine fleet.

Malorny (*2366*) in 1948 gave a report on measurements of carbon monoxide in the air of small submarines of the German Navy. In these one-man submarines fatal carbon monoxide poisoning occurred repeatedly in craft equipped with gasoline engines. The exhaust gases from these engines have a high carbon monoxide content, and the slightest leakages of the exhaust line in the confined spaces permitted the accumulation of dangerous concentrations of carbon monoxide. It was unexpectedly found that in craft operated with electric motors toxic concentrations of carbon monoxide were also found if the electric charge was too high. Whether this was due to sparking of the brushes or heating up of insulating material is not entirely clear. Schaefer (*2367*) in 1948 similarly drew attention to the danger in snorkel operations of the addition of carbon monoxide to the submarine atmosphere from the engines and stated that subtoxic and sometimes toxic concentrations of carbon monoxide developed.

Ellis (*2364*) gave an account in 1947 of another potential hazard from carbon monoxide in submarine operations. A torpedo motor started by accident when the torpedo tube of a submarine was being loaded at Malta in May 1941. It filled the torpedo compartment with exhaust fumes. An officer entered the compartment to rescue one of his men who had collapsed. The officer lost consciousness and was exposed to the toxic environment for 6 to 10 minutes. The officer was delirious after recovering consciousness and suffered from mental confusion for a long time. For many days he was completely blind. His vision then returned gradually. He was still unable to write for 2 months after the incident, partly because incoordination of fine movements and partly because of loss of memory and word pattern. Later he made a complete recovery. The man rescued from the compartment died later. A similar incident followed the firing of a practice salvo of torpedos at Malta later in the same year, when several of the torpedo firing party were overcome.

Solandt and Bunker (*2368*) reported in 1944 that under normal and blackened ship conditions the average level of carbon monoxide in the engineroom of "Fairmiles"-class vessels in the Royal Canadian Navy does not rise significantly above 0.009 percent. The authors stated that this level does not constitute a danger. Some cases of carbon monoxide poisoning were reported which were stated to be due to defect in the exhaust system with leakage of exhaust fumes.

2364. Ellis, F. P. The hazards of toxic gases in warships excluding agents of chemical warfare. *J. R. nav. med. Serv.*, 1947, *33:* 25–37. [R]

2365. Malorny, G. Carbon monoxide on submarines. pp. B: III–1—B: III–49 in: *Monograph on submarine medicine, Folio III,* Germany. U. S. Zone. Office of naval advisor. 1948.

2366. Malorny, G. The development of carbon monoxide on minature submarines (one man submarines). pp. B: IV–1—B: IV–24 in: *Monograph on submarine medicine, Folio III,* Germany. U. S. Zone. Office of naval advisor. 1948.

2367. Schaefer, K. E. Technical influences. I. Carbon monoxide, admixtures of the air, and trace substances. pp. B: I–35—B: I–38 in: *Monograph on submarine medicine, Folio I,* Germany. U. S. Zone. Office of naval advisor. 1948.

2368. Solandt, D. Y., and M. L. Bunker. Investigation of carbon monoxide hazards in naval vessels. Canada NRC. Proceedings of third meeting of associated committee on naval medical research. *Project C4076,* 15 May 1944, 9 pp. [P]

(c) Clinical Picture, Functional Changes, and Pathological Effects of Carbon Monoxide Poisoning

Carbon monoxide poisoning continues to be a potential hazard in industry as well as in submarine operations. After prolonged moderate exposure to carbon monoxide, there may be symptoms of acute intoxication, or symptoms of chronic carbon monoxide poisoning may develop without preceding acute intoxication symptoms. There may be headache, lassitude, drowsiness during the day, insomnia at night, irritability, loss of memory, vertigo, tremor, paresthesiae, and slight confusion. There may also be such symptoms as palpitation, precordial pain, dyspnea, colic, attacks of diarrhea, polyuria, impotence, and reduced tolerance for alcohol. There may be attacks of elevated temperature and disturbances of vision and hearing. Grut (*2390*) drew attention to the importance of differentiation of chronic carbon monoxide poisoning from recurring acute intoxication, and from the sequele of severe acute intoxication. In the course of studies carried out in English motorcar factories to determine the risk of carbon monoxide intoxication of workers, Feil (*2387*) reported in 1948 that the highest blood concentrations of carbon monoxide were detected among those workmen in the heating section, workers in foundries, truck drivers, and those supervising gas production. Among those working in parts of factories not particularly exposed to carbon monoxide intoxication, 83 percent of the workers had a blood carbon monoxide concentration of less than 0.6 cu. cm. per 100 cu. cm. of blood and only 4 percent had more than 1 cu. cm. of carbon monoxide per 100 cu. cm. of blood. Feil reported that a high content of carbon monoxide in the blood does not necessarily imply industrial poisoning. After a slight inhalation of gas there may be a transient carbon monoxide hemoglobinemia without injury to the health. He stated that chronic carbon monoxide poisoning can be affirmed only if carbon monoxide is found in the blood in considerable amounts several weeks after cessation of the dangerous occupation.

Bonnevie and Grut (*2374*) reported in 1948 that 90 percent of workers in foundries showed acute symptoms on the molding day while only slight symptoms of chronic carbon monoxide poisoning were encountered. This the authors attributed to the short and infrequent exposure. They encountered few chronic and acute cases in gasworks, and then only under defective outdated working procedures. After moderate exposure to carbon monoxide gas for 8 hours daily, 8 out of 15 female workers showed symptoms of chronic intoxication which disappeared after ventilation improvements. In locomotive running sheds and tunnels the air may contain high concentrations of carbon monoxide causing acute symptoms, but generally chronic intoxication does not occur. The authors reported that although 42 percent of bus drivers showed symptoms of acute intoxication, the occurrence of chronic carbon monoxide poisoning was not greater than in controls. For a further study of carbon monoxide poisoning in drivers or conductors, a paper by Peloquin (*2403*) published in 1951 may be consulted.

Chinn (*2380*), in a paper published in 1949, indicated the potential hazard of carbon monoxide poisoning in workers employed in airplane-engine repair shops. In 11 workers exposed to concentrations of less than 0.005 percent of carbon monoxide, there was no significant increase in the carboxyhemoglobin concentration in the blood after a normal 8-hour working day. In those workers exposed to an air concentration of 0.005 to 0.015 percent carbon monoxide, there was an average increase of 4.1 percent carboxyhemoglobin observed in the blood at the end of the day. These latter carbon monoxide concentrations in the air were found in poorly ventilated areas of the engine test section, the pickup line, and the engine storage room. Among those workers breathing less than 0.005 percent carbon monoxide in the air, no blood samples contained more than 6 percent carboxyhemoglobin. Among the persons breathing 0.005 to 0.015 percent carbon monoxide, 77 percent had carboxyhemoglobin concentrations exceeding this figure; 54 percent had over 8 percent carboxyhemoglobin; 17 percent had over 10 percent carboxyhemoglobin. Chinn reported that about 30 percent of all workers in this study claimed occasional or recurring headaches which were attributed to the working conditions.

Kugelberg (*2394*) in 1946 investigated 215 cases of carbon monoxide gas injuries, mainly among bus drivers in Stockholm. In at least 91 cases there was fusion reduction and conversion weakness leading to temporary diplopia and error in judging distances. In some cases there was weakness of accommodation, but no case of limitation of the field of vision, color discrimination, or any reduction of vision or ordinary paralysis of the eye muscles. Almgren (*2369*) in 1950 stated that the symptoms of carbon monoxide poisoning may be subjective and that there may also be definite ophthalmological signs present. In 197 cases of carbon monoxide poisoning with opthalmological findings at the author's clinic, 78 showed conversion defects, 69 showed convergence and fusion disturbances, and 50 fusion disturbances only. A followup study

of 66 cases revealed that these disturbances lasted as long as 6 months, 2½ years, or longer. A case was reported in 1951 by Fink (*2388*) of a 30-year-old white man who accidentally inhaled a quantity of illuminating gas from a faulty heater who, after a period of unconsciousness for 2 days, was afflicted with complete blindness, a weakness in the right upper extremity, and a depression of mental functions. During the following weeks, there was an improvement in vision and motor capacity. After the condition had become static, opthalmological examination revealed marked loss of visual acuity in each eye, with good color perception and active pupillary responses. The visual fields were markedly constricted. Restriction of the visual field following carbon monoxide poisoning in a driver continually exposed to carbon monoxide was also reported by Mercier (*2401*) in 1947. In this case, there was also a reduction in dark adaptation. Halperin, Niven, McFarland, and Roughton (*2391*) in 1947 reported an investigation of the comparative and the combined effect of carbon monoxide and hypoxic hypoxia on human visual intensity discrimination. In previous studies they had found that the measurement of the visual, intensity discrimination thresholds at a low level of illumination provide a sensitive, useful, and precise quantitative index of the physiological disturbances resulting from oxygen deprivation, and they applied the same technique in measuring the defect of small concentrations of carbon monoxide. They report that a given increase in the percentage of carboxyhemoglobin in the blood at sea level produces an effect approximately equal to that of a comparable decrease in the percentage of oxyhemoglobin due to hypoxic hypoxia. At simulated altitudes, a given percentage of carboxyhemoglobin produces an impairment equivalent to a further ascent which would cause an equal additional decrement in the percent of oxyhemoglobin. They have stated that the visual threshold is much more sensitive to carbon monoxide than are other physiological functions so far investigated. The authors found in a study of the recovery from carbon monoxide that inhalation of pure oxygen was more beneficial than inhalation of air in producing recovery. In a further study, McFarland, Niven, and Halperin (*2400*) in 1948 found that carbon monoxide was significantly effective even in small quantities in accentuating the effect of hypoxia. The change in oxygen tension of the blood was shown to be the determining factor in the elevation of the visual threshold. This was true whether it was associated with a loss in the oxygen-carrying capacity of the blood due to saturation with carbon monoxide, or a loss in the arterial oxygen saturation due to altitude, or to a combination of both factors. The saturation of the blood with carbon monoxide therefore results in defects equal to those caused by lowered arterial oxygen saturation of the same magnitude.

During World War II, a shortage of gasoline in the Scandinavian countries led to the use of carbon monoxide for motorcar power. This gave rise to large numbers of cases of carbon monoxide poisoning. Lumino (*2398*) reported in 1948 a total of 700 patients exposed to the influence of gases, especially carbon monoxide, in daily work and who were examined in the otolaryngological clinic of the University of Helsinki between 1 December 1945 and 31 May 1947. Of these, 263 suffered with chronic carbon monoxide poisoning. Detailed examination revealed hearing deficiency in 78.3 percent of all patients with chronic carbon monoxide poisoning, and 26.7 percent in patients having no definite objective symptoms of poisoning. The hearing loss dropped steeply between 1,000 and 2,000 cycles, and when the vibration rate was increased the hearing decreased steadily. Although the audiometric examinations revealed defective hearing in 78.3 percent of the patients tested, only 47.9 percent complained of reduction in hearing. Followup examination showed an improvement in auditory acuity in 26.7 percent of the cases. Improvement was always slight and occurred chiefly in those patients with only a slight initial hearing disturbance. In 10.7 percent of the cases, hearing returned to normal. Lumio concluded on the basis of these studies that carbon monoxide poisoning is frequently responsible for hearing impairment. Lumio further reported in 1948 (*2399*) that followup examinations 1 to 3 months later in some cases revealed subjective improvement in hearing, but no great improvement in the audiometric findings.

The symptoms of chronic carbon monoxide poisoning have been reported by Bourguignon (*2376*) in 1950. This author also described audiometric and other tests for chronic carbon monoxide poisoning. The poisoning effects of carbon monoxide particularly involved the central nervous system. There may be a disturbance of intellect, behavior, and consciousness with maniacal shouting, extreme restlessness, and struggling. The basal ganglia may be affected, and there may be hypertonia, increased or absent deep reflexes, clonus, and bilateral Babinski responses. Corkhill (*2381*) in 1947 commented upon cerebral edema with rise of cerebrospinal fluid pressure in these cases, and he recommended intravenous injections of 100 cu. cm. of 15 percent

saline solution to relieve headache and mental confusion. Four cases of carbon monoxide poisoning, showing characteristic extrapyramidal rigidity resembling Parkinson's syndrome, were described in 1949 by de Lehoczky (*2395*). These cases were also characterized by mental confusion and dementia. Pathological examination revealed a bilateral softening of the globus pallidus. In one case there were minimal lesions in the cerebral cortex, while in others there were severe alterations, not specifically localized but observed diffusely in nerve cells. Wohlfart, Gullberg, and Swensson (*2411*) stated in 1947 that subjective sensations are noted when the carboxyhemoglobin level reaches 30 percent. A saturation of 50 percent usually connotates mental involvement with cerebral as well as cardiac lesions. The author has discussed cases of Parkinsonism, hyperkinesis, hemiplegia, nystagmus, severe loss of equilibrium of the vestibulspinal type, and confusion. All of these cases have been attributed to chronic carbon monoxide poisoning. In a study of carbon monoxide poisoning in Finland between 1940 and 1947, Sumari (*2407*) reported in 1948 on the examination of 2,139 persons working in carbon monoxide-contaminated environments. In these cases arterial blood pressure was found to be above normal in 30 percent. Asymmetry and exaggeration of the reflexes with slight disturbances of the sensory and the sympathetic nervous systems were found in 70 percent. Vestibular disturbances were seen in 56.1 percent, and 67.7 percent of the cases had bilateral symmetrical deficiency in hearing. About 80 percent of the cases showed constriction of the visual field, particularly to blue light. The most commonly observed neuropsychiatric disturbance was a so-called toxic neurastenia. In followup examinations it was ascertained that in mild cases the symptoms disappeared in 1 to 4 months. In those cases of medium or moderate severity the symptoms disappeared in 6 months, and in the severe cases there were residual subjective and objective symptoms.

A report by Zahle (*2412*), published in 1947, indicates that peripheral neuritis is a rare but important sequel to acute carbon monoxide poisoning. Zahle's report is based upon a review of the literature and a study of his own material comprising 1,308 cases. Zahle concluded that peripheral nerve lesions following carbon monoxide poisoning most often affect the branches of the sciatic nerve.

Regarding psychiatric complications of carbon monoxide intoxication, Benon (*2372*), reported in 1949, considered that the first effect of carbon monoxide poisoning was a psychic and muscular asthenia. This condition, the author stated, dissipates gradually and is replaced by a hyperasthenia, sometimes with manic excitation, and this may give way to a periodic manic psychosis referred to by the author as a periodic dysthenia. Courville (*2382*) stated in 1948 that the danger of psychotic reaction or pyramidal or extrapyramidal disabilities is greater if the coma lasts longer than 36 hours.

Cardiovascular changes in acute carbon monoxide poisoning have been reported by Loeper, Varay, Cottet, and Leveille (*2397*) in 1947. In 17 cases of acute carbon monoxide poisoning, the authors found no evidence of angina pectoris. In one patient there was a transitory hypertension, while in two the arterial pressure remained essentially normal. In the others there was a hypotension. In some cases, the heart was abnormally slowed and in others there was tachycardia. Occasional extrasystoles were observed. There were many and variable electrocardiographic changes, the outstanding ones being disphasic changes in the P-wave, enlargement of the QRS complex, and flattening of the T–wave. It was found that prognosis depends upon individual predisposition, and is more grave in the presence of circulatory defects. In 29 cases of renal involvement following carbon monoxide poisoning, the authors found elevated blood urea nitrogen in 14 patients. Urinary examination disclosed but a few cases with albumin, casts, or red cells in the specimens. In two cases the elimination of PSP was reduced. It was concluded that the renal impairment in carbon monoxide poisoning is a result of renal asphyxia. Dahlstrom, Obreschkow, and Sjostrand (*2383*) reported in 1947 a comparison between the effects of carbon monoxide poisoning and inhalation of air with low oxygen content upon respiration, circulation, alkaline reserve of the plasma, and the patellar reflex in normal subjects and in cases of "chronic producer gas poisoning." Generally speaking, the effects were comparable. Similar findings have been reported by Swann and Brucer (*2408*) in 1949. For case histories of acute carbon monoxide poisoning with sample electrocardiograms, the reader is referred to a paper published in 1948 by Borst and Otten (*2375*).

The effects of experimental carbon monoxide inhalation in dogs upon peripheral vasomotor reactions have been reported in 1948 by Binet and Burstein (*2373*). In the perfused paws of dogs with the innervation intact, carbon monoxide inhalation resulted at first in an intense vasoconstriction, stated by the authors to be of central origin, giving way in the terminal phase to an equally intense phase

of dilatation. This latter phase was considered by the authors to be of humoral origin. In 1948, Sjostrand (*2405*) investigated the effect of carbon monoxide upon the diameter of the blood vessels in the pia mater. A glass window was mounted in the cranial wall of cats under light dial or ether anesthesia, and through this window the effect of carbon monoxide administered via the lungs upon the diameter of the blood vessels in the pia mater was observed directly with an ocular micrometer. The brain volume was estimated by determining the distance between the brain surface and the window surface. Intracranial pressure was measured by a water manometer connected to a cannula fastened into the cranial window. During absorption of carbon monoxide, the diameter of the blood vessels in the pia mater enlarged. The brain increased in volume and the intracranial pressure rose. After the administration of carbon monoxide, the brain volume and the diameter of the blood vessels slowly decreased approximately to their original level. The intracranial pressure, however, fell considerably below the prestimulation level. These observations are considered by the author to explain the headaches accompanying carbon monoxide poisoning and other very profound effects which this gas may have upon central nervous functions.

Asmussen and Knudsen (*2370*) reported, in 1943, studies on acute, moderate carbon monoxide poisoning in two normal men (25 to 32 percent carboxyhemoglobin in the blood). In these investigations, it was found that the relative cell volume of the blood as well as the plasma protein concentration were augmented after inhalation of carbon monoxide, suggesting a leakage of fluid from the vessels, presumably associated with peripheral vasodilatation. An increased rate of filtration could not be detected in the lower extremity. The concentration of glucose and lactic acid in the blood was unaffected by this degree of carbon monoxide intoxication so long as the subject remained quiet. In moderate work, the concentration of lactic acid increased, whereas the blood-sugar level remained normal. Glucose tolerance was unaffected by this degree of carbon monoxide poisoning. In a series of 17 cases of chronic carbon monoxide poisoning, Helve (*2393*) in 1949 found no striking differences from normal in the figures for blood phosphorus in various forms or cholesterol.

Cameron and Collins (*2377*) reported in 1946 a study of reproduction and lactation in albino rats during prolonged exposure to carbon monoxide. Adult female rats were exposed to sublethal amounts of carbon monoxide twice every 24 hours for 12 to 24 days. These animals gave birth to normal litters, but histological examination of the gonads of the exposed rats revealed extensive damage and degeneration. Females in which lactation was inhibited recovered before the next litter was produced. The same authors (*2378*) in 1948 reported placing male rats in an atmosphere consisting of 20 percent carbon monoxide and 80 percent room air for 1 to 2 minutes every 24 hours. At sacrifice on the 21st day there was failure of spermatogenesis, with very few spermatids and spermatozoa found in the testes.

For other studies of pathological changes in carbon monoxide poisoning, papers by Fornari (*2389*) 1949; Moniatte, Schwartz, Treussard, Malhuret, and Alt (*2402*) 1949; and Tosetti (*2409*) 1948, may be consulted. According to Lhermitte and De Ajuriaguerra (*2396*) 1947, the changes in the brain in carbon monoxide poisoning differ widely, depending upon the time elapsed between the exposure and the time of death. In those cases in which death occurred rapidly, the picture is characterized by hemorrhages, necrobiosis, necrosis, and edema. These changes may involve primarily the basal ganglia, but also the subcortical white matter, the hippocampus, the substantia nigra, and the cerebellum. Changes in the vascular network with infiltration of the walls by neutral lipids and by a peculiar substance containing iron salts, calcium, and lipids may be observed in cases in which the poisoning continues for a prolonged period or in which death is delayed. A diffuse demyelination of the entire white matter of the brain similar to Schilder's disease may be observed in cases in which death occurs after a long period of remission. It is suggested that in carbon monoxide poisoning there is, in addition to the anoxic factor, a toxic factor which affects the neuroglia and the vascular network. Ceresa (*2379*) in 1948 examined the central nervous system of a patient with acute carbon monoxide poisoning who died 24 hours after exposure. Comparing the findings in this case with another patient who died 26 days after intoxication, the author concluded that the alterations within the nervous tissue are not determined by a direct action of carbon monoxide on the nerve cell, but by asphyxia caused by vasoconstriction resulting from the carbon monoxide. Pathological changes in the brain of a 33-year-old man dying 3 months after exposure to carbon monoxide were described in 1951 by Fazekas and Gereb (*2386*). They described ganglion-cell changes in the cerebral cortex and in the basal ganglia, with perivascular changes and marked gliosis. There was widespread demyelination and fatty degeneration. Regarding the pathological mechanism of carbon monoxide poisoning,

the author considered that anoxia is the primary factor.

For other studies of the clinical picture, functional changes, and pathological effects of carbon monoxide poisoning, the reader is referred to papers by Asmussen and Knudsen (*2370*) 1940, Asmussen and Vinther-Paulsen (*2371*) 1950; Doumer and Merlen (*2384*) 1946; Enzer (*2385*) 1946; Hamburger, Collins, Shaver, and Gall (*2392*) 1949; Helve (*2393*) 1949; Perrin (*2404*) 1949; Sklyanskaya (*2406*) 1946; Vollmer, King, Fisher, and Birren (*2410*) 1945.

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2404. Perrin, M. Granulocytopenie consécutive à une intoxication oxycarbonée prolongée et discontinué. *Paris méd.*, 1949, *39:* 461–462. [CH]

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(d) Mechanisms of Carbon Monoxide Poisoning

A major action of carbon monoxide on the body depends upon interference with the oxygen transport mechanism in the blood. Pappenheimer (*2417*) in 1947 stated that moderate, acute carbon monoxide poisoning is believed to be the result solely of the effect of carbon monoxide on the equilibria between oxygen and hemoglobin. However, Lilienthal (*2415*) pointed out in 1951 that a wide selection of biological processes other than the oxygen-hemoglobin relationship is affected by carbon monoxide. Evidence is to be found in the literature that carbon monoxide may exert a direct toxic action upon the heart, for example. It is well known that carbon monoxide poisoning produces selective lesions in the central nervous system, and the mechanism for such selection as, for example, the special vulnerability of subcortical ganglia is not clear (Barthe and Paris (*2413*) 1949, and Van der Horst (*2414*) 1948). Pappenheimer (*2417*) has stated that the partial pressure of carbon monoxide necessary to produce a given percentage saturation of carboxyhemoglobin is 1/200 of the partial pressure of oxygen necessary to produce the same percentage saturation of oxyhemoglobin. Until recently it was believed that the rate of absorption of carbon monoxide by the blood was close to the maximum possible rate, but evidence indicates that it is approximately one-half the maximum possible rate. Elimination of carbon monoxide from the blood is stated to take place entirely by diffusion from the lungs. Evidence has been adduced that carbon monoxide in moderate amounts is not metabolized.

Lilienthal (*2415*) stated that many animal tissues, especially cardiac and skeletal muscle, can oxidize carbon monoxide to carbon dioxide. Recent studies have helped to deepen our understanding of the Douglas-Haldane blood-gas laws and to reveal the mechanisms of tolerance to carbon monoxide. Lilienthal, Riley, Proemmel, and Franke (*2416*) in 1945 reported on the relationship between carbon monoxide, oxygen, and hemoglobin in the blood of man at altitude. Three male subjects were studied at varying pressure altitudes while in equilibrium with inspired gas mixtures containing from 0.005 to 0.015 percent carbon monoxide. The distribution of carboxyhemoglobin, oxyhemoglobin, and reduced hemoglobin and their related gas tensions confirmed in vivo the fundamental laws first defined by Haldane for the equilibria obtaining in vitro. A simple rearrangement of the Haldane equation makes possible an accurate prediction of the amount of carboxyhemoglobin obtaining when man is in equilibrium with a carbon monoxide-contaminated atmosphere at any given altitude. The total barometric pressure was found to play no role in the distribution of carbon monoxide and oxygen at equilibrium. It appears that the hemoglobin of individuals who smoke does not differ from that of nonsmokers in its affinity for carbon monoxide and for oxygen. The symptoms produced by carbon monoxide are proportional not only to the blood concentration of carboxyhemoglobin but also to the duration of exposure to a given concentration. Sroka (*2419*) in 1951 stated that a volume percentage of 0.02 carbon monoxide replaces 12.5 percent of oxygen in the circulating blood in the form of carboxyhemoglobin. Carbon monoxide concentrations below this level may be considered harmless even over extended periods. Air containing 0.05 percent carbon monoxide puts approximately 30 percent of the hemoglobin in the blood out of action as far as its oxygen-carrying capacity is concerned. It is reported that symptoms arise when 18 to 20 percent of the hemoglobin

has been converted into carboxyhemoglobin. Inhalation of 0.1 percent carbon monoxide for 1 hour results in a conversion of 50 percent of the hemoglobin into carboxyhemoglobin, giving rise to a critical anoxia. The limit of tissue viability is believed to have been reached when 70 percent of the hemoglobin is bound as carboxyhemoglobin. This dangerous limit is attained when 0.4 percent carbon monoxide in air is inhaled for 25 to 30 minutes.

For further reports on the mechanism of action of carbon monoxide, the reader is referred to papers by Pitts and Pace (*2418*) 1944 and Wallgren (*2420*) 1950.

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2415. Lilienthal, J. L., Jr. Carbon monoxide. *J. Pharmacol.*, 1950, *99:* 324–354. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 487. Abstr.

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(e) Carbon Monoxide Uptake, Absorption, and Elimination

Pace (*2436* and *2437*) in 1945 constructed a nomograph for the estimation of the uptake of carbon monoxide by flying personnel breathing air up to altitude of 15,000 feet. The data required are toxic concentrations of carbon monoxide, altitude, and exposure time. The original nomograph was modified so as to make it possible to estimate the carbon monoxide uptake when personnel breathe varying quantities of ambient air containing carbon monoxide through a diluter demand regulator. In 1945, Lilienthal and Pine (*2434*) reported a study of the effect of oxygen pressure on the uptake of carbon monoxide by nine subjects at sea level and at altitude. Seventy-eight separate observations were made on 8 men and 1 woman. The duration of exposure to the carbon monoxide mixture varied from 20 to 66 minutes, and the variety of partial pressures of oxygen in the inspired air was used. In accordance with the laws of combination of carbon monoxide with hemoglobin in the presence of oxygen, the rate of uptake of carbon monoxide is inversely proportional to the partial pressure of oxygen. Using a formula decided on by the authors, the rate of uptake of carbon monoxide may be predicted with considerable accuracy for sea-level and altitude conditions. The total barometric pressure plays no discernible role in the uptake of carbon monoxide. The authors stated that the effect of minimal hypoxia due to altitude sums with the effect of small amounts of circulating carboxyhemoglobin to produce moderately severe symptoms of hypoxia. The same authors (*2433*) concluded that the correct use of oxygen equipment under normal conditions should prevent undue effect of carbon monoxide in aircraft.

Goldman (*2430* and *2431*) in 1947 constructed formulae for determining the rate of uptake of carbon monoxide by man. The rate of uptake is linear with time up to about one-third of the equilibrium value of carboxyhemoglobin in the blood. For this range the rate depends on the alveolar diffusion coefficient and the alveolar respiratory minute volume, as well as the ambient gas concentration. If an individual is exposed to an atmosphere containing carbon monoxide, his blood carboxyhemoglobin concentration increases at first linearly with time as stated, but more slowly as equilibrium is approached. It most often occurs that these equilibrium values are so high as to be dangerous, and it is thus of practical importance to deal primarily with the initial portion of the absorption curve. A formula is given which explains the fact that somewhat less than one-half of the carbon monoxide inhaled is absorbed into the blood. In vitro studies reported in 1947, Pace, Strajman, and Walker (*2438*) found that a 50-percent suspension of finely divided blood-free rat or guinea-pig liver in Tyrode's solution took up essentially no carbon monoxide when the suspension was shaken with this gas. It appears that there is no material in the liver capable of taking up sufficiently large amounts of carbon monoxide to explain the temporary retention of carbon monoxide by the liver in the intact animal. The authors describe a new type of Geiger-Muller counter tube for in vivo detection of gamma radiations by which it is possible to measure the disappearance curves of tagged

carbon monoxide in human subjects simultaneously in various parts of the body, including the heart, liver, and thigh. Preliminary studies indicated that in addition to fast and slow components observed in the heart and the liver, it is possible to resolve a third, very fast component with a half time of 0.28 to 0.88 minute. The authors believed that the very fast component and the fast component represent mixing phases in the disappearance curve, and that the slow component represents the true elimination of carbon monoxide from the blood via the lungs. No retention of tagged carbon monoxide in the liver was observed when doses of 80 cu. cm. or less of inert carrier carbon monoxide were used. This was presumed by the authors to indicate that the temporary retention of carbon monoxide by the liver is due to a transient local hypoxemia with an engorgement of the liver with blood.

In a study of the rate of carbon monoxide uptake by the blood, Behnke, White, Consolazio, and Pace (*2421*) in 1943 exposed 26 men on 42 occasions to various concentrations of carbon monoxide in air from 5 to 20 parts per 10,000. They found that in blood concentrations up to 35 percent carboxyhemoglobin, the uptake apparently follows a straight line. The principal factors affecting the rate of carbon monoxide accumulation in normal men were expressed quantitatively in an equation based upon experimental data. A simplified form of the equation for use as a gross approximation was obtained as follows:

$$\text{Time of exposure (in minutes)} = 200 \times \frac{\text{Percent carboxyhemoglobin}}{\text{Minute volume of respiration (in liters)} \times \text{parts of carbon monoxide per 10,000}}$$

In the application of this equation, if the carboxyhemoglobin is limited to 20 percent, and the minute volume is limited to 18 liters, i. e., in moderate exercise, then 20 parts per 10,000 of carbon monoxide can be breathed for 11 minutes; 15 parts per 10,000 can be breathed for 15 minutes; 10 parts per 10,000 can be breathed for 22 minutes. A constant amount of carbon monoxide is removed from tidal air throughout the course of the exposure. Therefore, the quantity of carboxyhemoglobin present in the blood does not appear materially to influence further uptake of carbon monoxide, at least up to concentrations of 35 percent carboxyhemoglobin. The rate of uptake up to 35 percent saturation is therefore represented by a straight line and not by an exponential curve which holds for the absorption of many of the inert gases. Carbon monoxide is held in such close combination with hemoglobin that a steep diffusion gradient is apparently maintained between lung carbon monoxide and blood carbon monoxide until the carboxyhemoglobin saturation reaches a fairly high figure, at least above 35 percent. The blood flow through the lung capillaries does not appear to be a limiting factor under these conditions. The blood appears to be capable of assimilating all of the carbon monoxide available in the lungs at each breath. In 1945, Pitts and Pace (*2440*) reported 2 tests of 12 and 7 hours' duration, respectively, at sea level upon supine subjects breathing, by means of a demand system and an A–14 mask, carbon monoxide concentrations of 89 parts per million and 156 parts per million to determine the rate of absorption. The percentage saturation of hemoglobin with carbon monoxide was determined each hour. The subjects ventilated at a rate of approximately 6.7 liters per minute. After 12 hours of exposure to 89 parts per million of carbon monoxide, one subject had a carboxyhemoglobin concentration of 11.0 percent. The second subject exposed to 156 parts per million of carbon monoxide for 7 hours had a final carboxyhemoglobin concentration of 16.6 percent. The course of the respective carbon monoxide uptake curves indicated that during the time of exposure neither subject maintained final equilibrium with the carbon monoxide concentration being breathed.

For a study of special methods of computation of the diffusion of carbon monoxide and oxygen through the membrane of the red blood corpuscles and the subsequent diffusion and binding of these substances within the red blood corpuscles, the reader is referred to a report published in 1951 by Nicolson and Roughton (*2435*).

An experimental study of the fate of carbon monoxide in the body during recovery from mild carbon monoxide poisoning in man was reported in 1945 by Roughton and Root (*2441*). In normal men breathing oxygen or air, it was found that the carbon monoxide recovered from the expired air amounts to only 60 to 70 percent of that currently lost from the blood during the first hour after carbon monoxide administration. Independent theoretical calculations confirm the validity of this result, according to the authors. If the subjects continued to breathe oxygen for 4 hours after the carbon monoxide administration, about 96 percent of the carbon monoxide initially absorbed by the subjects was recovered in the expired air over this more prolonged period. It was inferred that the 30 to 40 percent fraction of the carbon monoxide lost from the blood during the first hour and unaccounted for in the expired air must have combined reversibly with hemoglobinlike pigments outside

the main bloodstream. Subsequently, as the blood carbon monoxide content falls, the carbon monoxide dissociated reversibly from these combinations, diffuses back into the blood and then into the expired air. The results of the 4-hour experiments confirm previous views stating that there is no significant loss of carbon monoxide through the skin, sweat, urine, or feces, or by oxidation or other forms of metabolism, in all events, in mild carbon monoxide poisoning and with an adequate oxygen supply. Experimental studies of the elimination of carbon monoxide from the human body with reference to the possible conversion of carbon monoxide to carbon dioxide were reported in 1945 by Tobias and Lawrence (*2444*), and Tobias, Lawrence, Roughton, Root, and Gregersen (*2445*). In these experiments several normal men were each given, via the lungs, a relatively large amount of radioactive carbon monoxide mixed with about 150 cu. cm. ordinary carbon monoxide. Thereafter, the subjects breathed oxygen for a period up to 1 hour during which their expired carbon dioxide was absorbed in soda lime. Tests of the latter for radioactivity showed that the carbon monoxide oxidized to carbon dioxide by the body under these conditions amounted to less than 0.1 percent of the carbon monoxide currently lost from the blood. The time course of the radioactivity in three parts of the body, namely, the thigh muscles, the region of the spleen and heart, and the region of the liver, was studied by placing Geiger counters over these regions. The curves for the muscles and for the spleen-heart areas could be reasonably interpreted in terms of the average amount of blood present in them at any given time, and the rate of blood flow. The liver curve, however, showed an unexpectedly high and prolonged initial phase difficult to explain completely in terms of amount of blood present at any given time and the rate of blood flow. The nature of the possible additional factor present in this region was discussed by the authors.

Evidence for the conversion of carbon monoxide to carbon dioxide by isolated tissues and by the intact animal was reported in 1948 and in 1949 by Clark, Stannard, and Fenn (*2424, 2425,* and *2426*). Various tissues of the frog were exposed to a gas mixture containing 80 percent carbon monoxide and 20 percent oxygen for periods ranging from 5 to 10 hours. The rate of gas consumption in the carbon monoxide-oxygen mixture and in air were measured in a respirometer. The radioactive isotope C^{14} was used in the carbon monoxide-oxygen mixture, and the amount of carbon monoxide burned to carbon dioxide was calculated from radioactivity measurements of the respired carbon dioxide. The amount of carbon monoxide burned to carbon dioxide was found to agree with the excess gas consumption in the respirometer, thereby showing that the excess gas consumption was due to the burning of carbon monoxide to carbon dioxide. The rate of carbon monoxide oxidation by frog tissue was found to be highest for heart muscle, next for skeletal muscle, low in nerve, and negligible in skin. The amount of carbon monoxide burned to carbon dioxide but retained within the tissues was found to be a small fraction of the total amount of carbon monoxide burned. Other reports by Clark, Stannard, and Fenn (*2425*) 1949, (*2423*) 1950, and (*2427*) 1950 and Clark (*2422*) 1950 give additional details of the experimental evidence in tissues and in animals for the conversion of carbon monoxide to carbon dioxide. In general, the technique used by these authors consists in measuring (1) the total gas consumed by the tissues or the animal in the presence of a carbon monoxide-oxygen mixture minus the amount of oxygen consumed in air over an equivalent period, and (2) the radioactivity of the carbon dioxide collected during exposure of tissues or animals to the carbon monoxide-oxygen mixture containing radioactive carbon monoxide and the calculation of the amount of carbon monoxide which would have been oxidized to produce the measured amount of activity in the carbon dioxide collected. Turtles over an 8-to-13-day period consumed from 30 to 52 percent of the carbon monoxide, while mice over a 4-day period used 0.24 cubic millimeter of carbon monoxide per gram body weight per hour. Mice were reported to convert 0.28 cubic millimter of carbon monoxide to carbon dioxide per gram of body weight per hour. The rate of conversion of carbon monoxide to carbon dioxide by mice was 10 times greater than would have been expected by a straight-line extrapolation from the findings in isolated muscles in an 80-percent carbon monoxide-20 percent oxygen mixture.

In an experimental study of the influence of age on carbon monoxide desaturation in man, Pace, Strajman, and Walker (*2439*) 1948 have found that the half time of desaturation of carbon monoxide from the blood shows a 1-percent increase for each increase in year of age of the subject. The authors consider that respiratory and circulatory changes must occur with increasing age which are reflected in the rate of gas exchange between the blood and the ambient air.

For further studies on carbon monoxide uptake, absorption, and elimination, the reader is referred to papers by Fox (*2428*) 1948; Gemmill, Bierman, Lilienthal, and Fugitt (*2429*) 1944; Gullberg and

Svensson (*2432*) 1946; Sjöstrand (*2442*) 1950; and Sjöstrand (*2443*) 1951.

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(f) Tolerance and Acclimatization to Carbon Monoxide

The circulatory adaptation to severe carbon monoxide poisoning for 10 days with blood concentrations of carboxyhemoglobin up to 46 percent was studied in dogs by Asmussen and Vinther-Paulsen (*2446*) in 1949. The authors found a slight increase in cardiac output together with an increase in hemoglobin concentration. The latter was attributed in part to an acute, probably splenogenic, increase and partly to a slow increase caused by the new formation of red blood corpuscles. In spite of these adaptative reactions, the venous oxygen tension was low in chronic carbon monoxide poisoning. Gorbatow and Noro (*2448*) reported in 1948 that rats and mice which were exposed daily to carbon monoxide in concentrations of 0.25, 0.4, and 0.5 percent became acclimatized easily to these concentrations,

so that in 8 to 15 days the tolerance was increased 2 to 4 times the control value. Only slight acclimatization to a concentration of 1 percent carbon monoxide was observed. An intermission of several days in the exposure diminished the tolerance. The longer the intermission, the greater the loss of tolerance. Polycythemia was observed with the acclimatization, but this later disappeared and there was increased tolerance without polycythemia. In the acclimatized animal there was noted no decrease in the percentage of carboxyhemoglobin in the blood. Clark (*2447*) in 1950 presented data indicating that mice exposed to concentration of carbon monoxide up to 0.15 percent for 3 weeks could survive an acute exposure to a simulated altitude of 34,000 feet much longer than mice unacclimatized to carbon monoxide. Conversely, mice that had been exposed to low oxygen, simulating an altitude of 18,000 feet for 3 weeks, were able to survive in an atmosphere containing 0.25 percent carbon monoxide for a considerably longer time than mice unacclimatized to low oxygen. In an attempt to determine the factors responsible for acclimatization to carbon monoxide and to low oxygen, the author found an increase in the oxygen capacity of the blood of about 60 percent, and in the hematocrit of about 85 percent in both the carbon monoxide and the low oxygen animals. The carbon dioxide capacity of the plasma was found to decrease for the mice exposed to low oxygen, but showed no change from the controls for animals exposed to carbon monoxide. Since the carbon dioxide capacity is a measure of the alkaline reserve, and the alkaline reserve is known to vary with the ventilation, the results seemed to indicate that mice in low oxygen environments hyperventilated, whereas those exposed to carbon monoxide exhibited no change in ventilation. The rate of oxygen consumption was measured on all the animals under normal atmospheric conditions and during acclimatization to carbon monoxide and low oxygen. The rate during acclimatization did not vary from that under normal atmospheric conditions. In none of these groups was there any significant alteration in acclimatization to low oxygen, although an increase in hemoglobin is a constant finding in acclimatization to high altitude. The results of these studies would seem to indicate that there are also other pertinent adjustments made by the animal during the process of acclimatization.

In a study of the nature of acclimatization occurring during repeated exposure of a human subject to atmospheres containing low concentrations of carbon monoxide Killick (*2450*) in 1948 subjected a man repeatedly to concentrations of carbon monoxide of 0.019 to 0.045 percent for 1 hour in an airtight chamber. Each exposure was prolonged until the carboxyhemoglobin percentage attained a steady value. Acclimatization was indicated by a diminution in the severity of symptoms and a discrepancy between the observed carboxyhemoglobin percentage at the end of exposure and the greater carboxyhemoglobin percentage obtained in vitro when the subject's blood was equilibrated with a mixture containing oxygen and carbon monoxide at the same partial pressure as in alveolar air. In this acclimatized subject there was no change in red blood count, proportion of reticulocytes, or in blood volume. Thus, there was acclimatization without evidence of a hematopoietic response. The author also indicated that there was no appreciable destruction of carbon monoxide in the body, and stated that the value of the constant for partition of hemoglobin between oxygen and carbon monoxide, as determined in vitro, remained unaltered as acclimatization developed.

For a study of safe human tolerance for high concentrations of carbon monoxide over short periods of time, reference may be made to a paper published in 1951 by Hall, Patterson, and Colehour (*2449*).

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(g) Treatment of Carbon Monoxide Poisoning

Several reports are on record in the literature on the value of intravenous administration of procaine hydrochloride in the treatment of asphyxia due to carbon monoxide. In 1943, Besancon and Laroche (*2453*) described the successful treatment of four cases of carbon monoxide poisoning with novocaine in amounts from 400 to 700 milligrams. These authors cited the use of novocaine in a case with coma following ablation of an intercranial tumor. In this case 5 cu. cm. of a 1-percent solution of novocaine was given, and the patient recovered. Amyes, Ray, and Brockman (*2451*) reported in 1950 the treatment of 23 patients with procaine hydrochloride injected intravenously after carbon monoxide poisoning. All of these patients showed neurological or

mental abnormalities. The usual dose of procaine hydrochloride was 500 milligrams given intravenously in 500 cu. cm. of 5 percent dextrose in water or isotonic saline solution. The solution was given over a 2-hour period. In each case a skin test for procaine sensitivity was carried out before injection. If the patient was conscious and there was no respiratory depression, an injection of 0.13 gram of sodium phenobarbital was given intramuscularly. Seventeen patients made good recoveries, while 6 died or did not fully recover. These six had received procaine administration late. Also, the average age of this latter group was 67. Moreover, they constituted a group more susceptible to hypoxia and also there were some who had had previous neurological disturbances or a history of coronary disorder. These cases are also discussed by Beckman (*2452*) in the 1950 *Yearbook of Drug Therapy,* published in 1951. Beckman pointed out that the earlier the procaine was given the better were the results.

Olsen, Marinacci, Ray, and Amyes (*2456*) in 1949 described several cases of asphyxia due to carbon monoxide treated by intravenous injection of procaine hydrochloride. A 27-year-old male patient had gone to sleep in a closed room with a lighted gas heater. The deep reflexes were hypoactive, abdominal reflexes were absent, and Babinski's sign was positive bilaterally. The temperature was 100.4° F., the pulse was 104, and the respiration 22. The patient was given 500 milligrams of procaine hydrochloride intravenously in a 1-percent solution in physiological saline. The blood pressure rose from 130/90 to 140/95. There was a restoration of normal cerebral rhythm as demonstrated by the electroencephalogram, and the patient was discharged improved after 3 days. A 61-year-old woman who had been poisoned with carbon monoxide was still moderately cyanotic after 24 hours of oxygen administration. There were choreiform movements, hyperkinesis, and quasipurposive motor activity. In addition to oxygen, the patient received a transfusion of 500 cu. cm. of whole blood on the day of admission and 10 cu. cm. of 1 percent procaine intravenously the following day. The patient left the hospital with no symptoms. The rationale for the use of procaine hydrochloride has not been adequately described in the literature cited. However, its value, if any, probably depends upon the central action of procaine in stimulating the central nervous system from above downward. As is well known, the first recognizable action of procaine is on the cerebral cortex and is manifested in restlessness and excitement, with some evidence of increase of mental power and capacity for muscular work. Procaine acts upon the medulla as a respiratory stimulant and also excites the vasomotor centers. The use of a drug for its central effect is fraught with danger since central stimulation is often followed by depression. Eventually, the medullary centers may be depressed and death may result from respiratory failure. Although procaine is stated to be the least toxic of all local anesthetics, it sometimes causes sympathetic effects in sensitive subjects. Death has been reported in the literature from the injection of as little as 0.01 to 0.13 gram of procaine. The use of barbiturates along with procaine makes for greater safety.

The literature on the use of oxygen in the treatment of patients asphyxiated with carbon monoxide can be only briefly alluded to here. There is some difference of opinion as to whether pure oxygen is preferable or whether a better result is obtained from a mixture of 93 percent oxygen and 7 percent carbon dioxide. Claim for the superiority of both has been made, but the recent trend is to regard the use of carbon dioxide-oxygen mixture as of questionable value in the treatment of carbon monoxide poisoning. In some forms of asphyxia, it is asserted that the use of carbogen may be actually harmful. Respiratory physiologists and anesthesiologists generally tend to prefer 100 percent oxygen to carbogen in artificial respiration, although many reports suggest that pure oxygen or carbon dioxide mixtures are equally effective. Reports indicate that the use of the carbon dioxide-oxygen mixture hastens the elimination of carbon monoxide from the blood. Vining, Whittenberger, and Wollack (*2462*) 1946 came to this conclusion in an experimental study of carbon monoxide poisoning in animals. In these experiments a mixture of 7 percent carbon dioxide and 93 percent oxygen was used for 10 minutes as inhalation therapy on goats as well as dogs, sustaining an arterial saturation of 60 to 80 percent carbon monoxide. The rate of elimination of carbon monoxide and the effect on the blood carbon dioxide levels, on blood pressure, and on minute volume of respiration were compared with similar data on two groups of goats and dogs similarly asphyxiated but treated with pure oxygen or room air. The animals treated with the carbon dioxide-oxygen mixture eliminated an average of 10 percent more carbon monoxide than those treated with pure oxygen. In the authors' experiments there was no evidence of respiratory or circulatory depression during the period of inhalation of the carbon dioxide-oxygen mixture or following its use. For a further report on the clinical use of carbogen in the treatment of cases of carbon monoxide poisoning, reference may be made to a paper

published in 1948 by Desoille, Griffon, Assouly, Feldstein, and Le Breton (*2454*).

Pace, Strajman, and Walker (*2457*) 1951 have found that the elimination of carbon monoxide from human subjects can be accelerated by breathing oxygen under high atmospheric pressure. In their experiments, 10 subjects, 5 males and 5 females, breathed a mixture containing 250 milliliters of carbon monoxide and 2 liters of air from a bag for 30 seconds. Each subject was then placed in a compression chamber and the ambient pressure raised to 2.5 atmospheres. Oxygen breathing was begun and the venous blood analyzed every 15 minutes for carboxyhemoglobin. In these experiments, the half time of carbon monoxide elimination was of the order of 20 minutes for the male subjects and faster in the females. These findings were compared with the half-time elimination values when the subjects breathed 20 percent oxygen and 100 percent oxygen at 1 atmosphere. In these latter experiments, the half-time elimination of carbon monoxide with 20 percent oxygen was 249 minutes, and for the 100 percent oxygen experiment 47 minutes. The elimination in the female subjects was 30 percent faster than in the males. Reference may also be made to the alleged benefit of ozone inhalation in lowering the carbon monoxide content of blood when carbon monoxide is present in the air. In an experimental study on white mice, Pitts and O'Neal (*2458*) 1948 exposed adult white mice to atmospheres containing physiologically tolerable concentrations of ozone (from 0.01 to 0.1 part per million) at two different concentrations of carbon monoxide; namely, 118 parts per million and 553 parts per million. Under these conditions the blood carbon monoxide saturation curves showed no effect whatever of ozone. The authors attributed previous positive results reported in the literature to experimental inadequacy.

Many of the questions at issue in the treatment of carbon monoxide poisoning have been settled by the work of Schwerma and his colleagues. Their studies include evaluation of methods of artificial respiration in conjunction with administration of pure oxygen or carbogen. Schwerma, Ivy, and Friedman (*2459*) in 1948 reported a comparative study of the effectiveness of several commonly used methods of resuscitation in dogs asphyxiated with commercial cylinder carbon monoxide diluted with air. Carbon monoxide concentrations of 0.3, 2, and 5 percent were used. One hundred and fifty-seven dogs were exposed to 0.3 percent carbon monoxide until the onset of the first respiratory gasp. Of 20 animals in this group receiving no treatment except removal from the asphyxiating chamber, three survived. Thirty animals were treated by manual artificial respiration with inhalation of 7 percent carbogen, and of these, 15 survived. A further 30 animals were treated with mechanical artificial respiration of the "suck and blow" type with 100 percent oxygen, and of these, 14 survived. Thirty animals were treated with mechanical artificial respiration of the "suck and blow" type with 7 percent carbogen, and of these, 15 survived. Thirty animals were treated with mechanical artificial respiration of the positive pressure type with 7 percent carbogen, and of these, 12 survived. Seventeen animals were kept in the asphyxiating chamber for 1 minute after the last respiratory gasp and were then treated with mechanical artificial respiration of the "suck and blow" type with 7 percent carbogen. None of these animals survived. Ten animals were exposed to 5 percent carbon monoxide until the onset of the first respiratory gasp. Except for one dog, which did not manifest air hunger, all were resuscitated with mechanical artificial respiration of the "suck and blow" type with 7 percent carbogen. Fifty-nine percent of all dogs exposed to 0.3 percent carbon monoxide longer than the mean time of 60.5 minutes survived, and 82 percent of the survivors suffered neurological sequelae of more than transitory duration. Thirty percent of the dogs exposed to 0.3 percent carbon monoxide less than the mean time of 60.5 minutes survived, and of these, 48 percent suffered neurological sequelae of more than transitory duration. From the survival data in these experiments, the authors concluded that artificial respiration induced by the mechanical resuscitators has no advantage over manual respiration with inhalation of 7 percent carbogen. In previous studies in which a large number of animals were asphyxiated with illuminating gas, it was found that mechanical artificial respiration was unquestionably more effective than manual methods. Since the experimental conditions were identical, except for the source of carbon monoxide, the authors considered that the differing results must be due to some difference in the action of the asphyxiating gas. The authors suggested that the carbon monoxide has a histotoxic effect based on the combination of carbon monoxide with iron-containing enzymes related to hemoglobin, and that the presence of some constituents in natural gas prevents or delays this combination and thus decreases the toxicity of carbon monoxide.

In 1948, Schwerma, Wolman, Sidwell, and Ivy (*2461*) reported further studies in which dogs were given various types of resuscitation treatment after exposure to air containing 0.3 percent carbon mon-

oxide until acute respiratory distress in the form of air hunger or gasping appeared. In these experiments, the rate of clearance of carbon monoxide from the blood of the dog was studied. The following methods of resuscitation were used: (1) manual artificial respiration with inhalation of air, (2) mechanical artificial respiration of the "suck and blow" type using 100-percent oxygen, (3) the same device using 7-percent carbogen, and (4) mechanical artificial respiration of the positive pressure type using 7-percent carbogen. In the authors' experiments no direct relationship was found between the concentration of hemoglobin present in the blood and the chances of survival from carbon monoxide asphyxia. The average difference in the hemoglobin values between the survivors (15.3 grams per 100 cc.) and the nonsurvivors (14.5 grams per 100 cc.) was stated to be suggestive, but not specifically significant, since individuals with high and low hemoglobin concentrations were present in each group. There was an evident and striking individual variation in the susceptibility to effects of carbon monoxide asphyxia. The mean carbon monoxide saturation in animals at the time of the first gasp was 74.3 percent. Twenty dogs with a saturation of 74 percent or less were exposed for an average of 52 minutes before showing the first gasp, whereas 21 dogs showing a saturation of 74 percent or more withstood the exposure for an average of 76 minutes. The latter group of animals were obviously more tolerant to carbon monoxide poisoning for some reason other than the hemoglobin content of the blood, and the answer to the question raised by this experiment is not evident in the data. The conclusion is that inhalation of oxygen is an efficient means of rapidly reducing the carbon monoxide content of the blood. The authors asserted also that administration of oxygen forces the dissociation of carboxyhemoglobin and thereby promotes rapid elimination of carbon monoxide. The only effects of administration of exogenous carbon dioxide are the slightly more rapid excretion of carbon monoxide and in some cases a more rapid restoration of respiratory movements. The significance of these effects has been exaggerated, according to the authors, while the much greater significance of adequate cardiac function has in large part been overlooked. Since carbon dioxide plays no demonstrable part in fortifying cardiac function, its addition to oxygen in the inhalation of the mixture confers no further value in resuscitation. It is, therefore, concluded that the carbon dioxide is an unnecessary therapeutic adjunct.

In view of the importance of cardiac support in the therapy of victims of carbon monoxide poisoning, Schwerma, Ivy, and Friedman (*2460*) in 1948 gave intracardiac injection of epinephrine and atropine in conjunction with 100-percent oxygen administration by a mechanical resuscitator to dogs asphyxiated with 0.3 percent carbon monoxide. The use of epinephrine and atropine appeared to confer an additional advantage, and the authors believed that this treatment was worthy of trial as a last resort in human cases of cardiac arrest following carbon monoxide asphyxia.

The literature on the use and design of gas respirators to protect against carbon monoxide in the air cannot be reviewed here. The reader is referred to a description by Forbes and Grove (*2455*) 1948 of a pocket-size gas respirator that protects the wearer against carbon monoxide in the air for one-half hour.

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(h) Carbon Monoxide Detection in Air and Blood

Methods for detection of carbon monoxide in the air and in the blood will not be discussed in detail, nor will the literature be exhaustively summarized. Reference is made to the section on gas analysis in air and blood (p. 2). Regarding methods for detection of carbon monoxide in the air, a classical method utilizes the hoolamite or activated iodine pentoxide indicator. The white hoolamite granules are changed to bluish green, then to violet brown, and finally to black, depending upon the concentration of carbon monoxide in the air. For references to this method, papers by Forbes and Grove (*2472*) 1937; Consolazio, Pecora, MacDonald, Collison, Kreuger, Platt, O'Neal, and Rae (*2471*) 1945; and Pitts (*2481*) 1947 may be consulted. The following papers deal with the hopcalite indicator: Mueller, Pope, Sharpe, Vollmer, and Walker (*2478*) 1944; Salsbury, Cole, and Yoe (*2484, 2485*) 1947; and Yoe and Lindsley (*2494*) 1944.

Shepherd (*2486*) in 1946 developed a colorimetric indicating gel for the rapid determination of small amounts of carbon monoxide in the air. This gel will detect and estimate less than one part of carbon monoxide in 500 million parts of air in approximately 1 minute. Field use requires a small, inexpensive apparatus without maintenance problems, and involves procedures so simple that untrained personnel can obtain reliable results. Yoe, Cole, and Salsbury (*2493*) 1943 have also described carbon monoxide indicators of the impregnated silica gel type. The determination of carbon monoxide in air by the use of red mercuric oxide has been described by McCullough, Crane, and Beckman (*2476*) 1948, and Beckman, McCullough, and Crane (*2465*) 1948. Other methods include a silver permanganate zinc oxide method described by Katz and Katzman (*2474*) 1949; an infrared analyzer described by Siebert (*2487*) 1948, and Nelson (*2479*) 1945; and methods using the absorption or fixing of carbon monoxide by hemoglobin solution described by Soucek (*2489*) 1949 and Chinn (*2469*) 1946. For other indicators, the reader may consult the following references: *2468, 2480, 2483,* and *2495.*

For a description of methods of estimation of carbon monoxide in the blood, the following references should be consulted: *2463, 2464, 2466, 2467, 2470, 2473, 2475, 2477, 2482, 2488, 2490, 2491,* and *2492.*

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2. ARSINE

Poisoning of submarine personnel by arsine is a hazard which is now of historical concern only. This is true because of improved industrial methods in providing lead-battery grids free of contamination with arsenic. Insistence upon the purity of the lead is essential in the protection of personnel and the virtual elimination of arsine poisoning in submariners should not blind us to the dangers involved. Rigid enforcement of material standards for batteries and of adequate ventilation of battery compartments is a continuing requirement.

Arsine is primarily a hemolytic agent. It is produced when an acid and a metal, either or both containing arsenic, are brought into contact, with a resulting liberation of nascent hydrogen which combines with arsenic to form the toxic gas, arsine. In a chapter on arsenic poisoning, McConnell (*2504*) 1951 called attention to arsine poisoning in galvanizing works, submarines (from battery plates or acid) or ships carrying ferrosilicon. Inhalation of arsine over a period of several hours in a concentration of 30 parts per million will cause poisoning and lethal doses range from 100 milligrams to over 500 milligrams. There are individual variations in susceptibility. The symptoms usually manifest themselves about 6 hours after inhalation of the toxic gas, and consist of malaise, vertigo, weakness, headache, nausea, and vomiting. There may be abdominal pain and diarrhea. A few hours later, hemoglobinuria or hematuria and albuminuria are observed. The pulse may be rapid and feeble, and the respiratory rate increased. Within a day or two, there may be a coppery cyanosis with jaundice. The leucocytes are not normally involved. There may be transitory toxic polyneuritis with pain or anesthesia, but there is usually no motor involvement. The condition carries a 30-percent mortality and in fatal cases, death occurs usually within a week. Oxygen should be administered immediately and inhalation of oxygen should be prolonged. Blood transfusion may be necessary. BAL (2,3-dimercaptopropanol) developed as an antidote to arsenical blister gases, appears promising in the treatment of arsenical poisoning. McConnell recommended that 3 milligrams of BAL per kilogram of body weight be given intramuscularly every 4 hours for the first 2 days,

followed by 4 injections on the third day, with injections twice daily for 10 days thereafter or until complete recovery.

Reed and Harcourt (*2507*) 1941 pointed out that arsine as such is not used in industry, but is a dangerous byproduct of several industrial processes. It is a hazard to acid dippers, hydrogen balloon workers, battery workers, and makers of bleaching powder and fertilizers. Much of the arsine poisoning in the United States occurs in workers cleaning out tanks and tank cars which have contained concentrated hydrochloric or sulfuric acid with arsenic as an impurity. Arsine is probably the most poisonous of all the inorganic gaseous compounds, and amounts ranging from 0.1 to 1.0 percent in air often prove fatal. These authors point out that it may take 6 to 36 hours to produce an effect, depending upon the size of the dose. They draw attention to the fact that arsine is a hemolytic poison and that the essential pathological process is a rapid extensive destruction of the red cells with cellular debris from the destroyed red cells clogging the capillaries and producing ischemia of certain organs. The symptoms are those associated with a destruction of red cells; namely, dizziness, nausea, general weakness, vomiting, epigastric pain, prostration, and death if poisoning increases. If the patient survives the first few hours, the urine may be bloody, and in 24 hours there may be jaundice with the red blood count as low as 2 million cells per cubic millimeter. Regarding treatments, the authors recommend that the patient be removed from the influence of the poison as quickly as possible and given continuous inhalation of oxygen until out of danger. If respiration is embarrassed, they recommend the addition of carbon dioxide to the respiratory mixture. They also suggest immediate blood transfusion, and as the patient recovers, massive doses of iron. For further general studies of arsine poisoning, the reader is referred to papers by Assouly and Griffon (*2496*) 1949, and Fourcade (*2498*) 1950. The paper by Assouly and Griffon is a particularly good bibliographical source.

For reports of clinical cases of arsine poisoning, the reader is referred to papers by Hawlick and Ley (*2499*) 1946; Lièvre, Bloch-Michel, and Solignac (*2503*) 1948; Spolyar and Harger (*2509*) 1950; and Wills (*2501*) 1948. These studies also reveal that arsine poisoning is an acute hemolytic process often fatal, and sometimes followed in nonfatal cases by a chronic involvement of the kidneys. Wills (*2510*) reported the case of a 51-year-old man who cleaned a Heroult steel furnace which contained drosses of calcium arsenide, calcium phosphide, and calcium carbide from a process treating manganese ore. The furnace had been empty for 1 month and the victim worked in the furnace for 3 hours. Medical examination the day before exposure had revealed that the worker was in normal condition. Signs and symptoms began on the day of exposure and there was dark, port-wine urine with muscular aches, slight fever, a parboiled redness of the skin, and acute redness of the sclera. The tongue was dry and coated, there was a metallic odor of the breath, and the temperature was 101.2° F. orally. The pulse was 86 and the blood pressure was 84/52, the normal on previous examination having been 112/80. There was mild tenderness in the midepigastric region. In the hospital, blood hemoglobin had fallen to 8 grams, or 51.5 percent. There were 2,350,000 red blood cells, and 14,450 white blood cells. Later, the red blood cell count fell to 1,500,000 and the hemoglobin to 38.2 percent. Daily whole-blood transfusions were given together with fluid orally, and 2,000 cu. cm. of 10-percent glucose in saline intravenously. Every 4 hours, 1.35 cu. cm. of BAL were administered intramuscularly. Diagnosis of blood destruction due to heavy metal poisoning was based on the findings of marked destruction of red blood cells with symptoms of anoxemia and anemia, urinary suppression, hemoglobinuria, and pulmonary edema.

Josephson, Pinto, and Petronella (*2500*) 1951 have reported electrocardiographic changes in human patients with arsine poisoning and have called attention to characteristic elevation of the T-wave in all leads from 2 to 12 days after arsine exposure. In four deaths occurring after arsine poisoning, the authors ascribed the fatal outcome to rapid myocardial failure. Pathological examination in two fatal cases revealed myocardial degeneration. This was ascribed either to the direct action of arsine on cardiac musculature, or to the action of metabolites (arsinites) formed from the reaction of arsine poisoning have been reported by Firket (*2497*) 1951; Moureau, Ponsart, and Warin (*2505*) 1951; and de Scoville (*2508*) 1949. In one case reported by Firket (*2497*), post-mortem examination revealed pulmonary parenchymal congestion; a flaccid, dilated heart with a pale myocardium; and a congested liver. Microscopically, there were extravasations of plasma into the pulmonary alveoli, red blood cells in the lumen of the renal glomeruli, and tumefaction of the renal epithelium. Firket considered that it is the excessive lowering of the arterial blood pressure which leads to the anuria, and not just the mechanical blockage of the nephrons. In the cases which came to autopsy, reported by Moureau, Ponsart, and Warin

(*2505*), there was icterus of the conjunctivae and pallor of the myocardium. The surface of the heart showed small hemorrhagic suffusions. There was pulmonary edema and pallor of the liver; the kidneys showed the classical picture of hemoglobinuria with albuminous precipitate and cellular debris in the intracapsular space. In a case in which death supervened in 54 hours, de Scoville (*2508*) indicated that the damage to the nephrons was generalized, but that the most significant lesions were localized in the distal convoluted tubules. The characteristic lesions in arsine poisoning are similar to those observed in nontraumatic muscular ischemic necrosis, crush syndrome, and burns. Apart from the tubular necrosis in the distal convoluted tubules, there were intratubular casts in the same portion. No gross interstitial edema was observed. The author considered that mechanical blockage produced by intratubular necrosis and precipitate could not alone account for the anuria. The possibility of diversion of blood from the renal cortex to the juxta-medullary region was discussed.

In a discussion of the mechanisms of the lethal action of arsine, Nau (*2506*) 1948 listed (1) the hemolysis of red blood corpuscules with the liberation of toxic arsenic-containing substances, (2) blockage of the kidney tubules by products of the hemoglobin breakdown, and (3) decrease of the oxygen-carrying capacity of the blood. The author also suggested that some arsine escapes red blood corpuscle fixation long enough to be carried to vital organs where its toxic effects are manifested. This corresponds to the conclusions of Levvy (*2501*) 1947–48 that the toxicity of arsine in the higher concentration ranges may in part be due to the action on vital organs of the unchanged gas reaching them in physical solution in the blood plasma. Arsine is believed to be lytic only under aerobic conditions. The mechanism of lysis is not known. Arsenic trioxide and arsenic pentoxide are stated by Nau (*2506*) not to be lytic. He calls attention to the fact that arsine inhibits the respiration of various organ tissue slices, including kidney.

In 1946, Kensler, Abels, and Rhoaes (*2502*) reported animal experimental studies on the treatment of arsine poisoning. These authors assumed that if compounds could be found which would effectively prevent the hemolysis of erythrocytes by arsine in vitro, or would protect the respiration of the tissue slices from inhibition by arsine in vitro, these compounds should be effective in the treatment of the clinical condition. Some dithiols were found to prevent the lysis of red cells by arsine in vitro when added 5 minutes after the cells had been exposed to the toxic gas. Some dithiols also protected tissue respiration from inhibition by arsine or by arsenite. Several dithiols were found to be effective in saving the lives of rabbits, dogs, and monkeys poisoned with arsine.

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3. BERYLLIUM

Beryllium is extracted from beryl ore which is mined in Brazil, Germany, Russia, India, and the United States of America. Since the 19th century, beryllium has been used as an alloy with copper, and is now also employed as an alloy with aluminum to make it resistant to corrosion and to increase resistance to stress and strain. Beryllium is also used in radio tubes, neon-sign tubing, and electric heating elements. Some of the first cases of pneumonitis

from beryllium were reported in the fluorescent lamp industry (*2522, 2528*).

A major source of information on beryllium poisoning is Vorwald's volume (*2538*) published in 1950. As Vorwald and others have pointed out, beryllium poisoning manifests itself in an acute form and in a chronic form. In acute beryllium poisoning, the clinical manifestations are dermal and respiratory. These are contact dermatitis, conjunctivitis, corneal burns, and ulcers. Regarding the respiratory effects, the symptoms vary from rhinitis to pneumonitis. Treatment for the acute manifestations is supportive with prevention of further exposure, absolute rest, and oxygen administration. Benadryl and pyribenzamine are stated to be sometimes beneficial. The chronic form of beryllium poisoning is characterized by the long latent period often seen between the last exposure to beryllium compounds and the development, sometimes years later, of respiratory symptoms. The clinical features of the chronic disease are dyspnea, loss of weight, and a chronic pulmonary granulomatosis. The diagnosis is established by ruling out pulmonary tuberculosis, silicosis, and Boeck's sarcoid. Hasterlik (*2525*) 1949 has pointed out that beryllium poisoning should be understood as a disease of the entire body, although the most prominent and incapacitating features are centered in the respiratory system. Beryllium poisoning has been produced by exposure to many beryllium compounds as well as the finely powdered beryllium metal. Tracer studies on animals with Be^7 indicate that a large and significant portion of the injected dose of a soluble beryllium salt is rapidly deposited in the bone, where it remains almost indefinitely. This finding of deposition of beryllium in the bone gives a clue to the mechanism of the delayed appearance of the disease. It is possible that various "trigger mechanisms" act to release beryllium stored in the bones into the general circulation. Hasterlik believes that it is not possible at present to set "safe" levels of concentration of beryllium in the air. It is known that exposure to air concentrations of a beryllium compound of 25 micrograms of beryllium per cubic meter of air has produced the acute form of the disease. This, then, represents a level which should never be permitted. The danger of beryllium poisoning in work spaces emphasizes the importance of continual air purification. Sax (*2531*) 1951 indicated that the maximal allowable concentration of beryllium in air in a working area is 2 micrograms per cubic millimeter of air. Vorwald (*2538*) has drawn attention to definite species differences in the susceptibility of the common laboratory animals to beryllium compounds inhaled experimentally. In studies on the dog, rabbit, guinea pig, mouse, hamster, and rat, mice were found to be most susceptible. There is striking pulmonary damage in all species with a consistant rise in the leukocyte counts in the dog, rabbit, and rat. None of the animal studies reproduces exactly the type of pulmonary lesion seen in the clinical disease in man. For further studies on the general problems of acute and chronic beryllium poisoning and the medical control of beryllium poisoning, the reader is referred to reports by Hardy (*2523*) 1949, and Tabershaw, Dustan, and Goldwater (*2534*) 1949.

The exact mechanism of the poisonous action of beryllium compounds is not known. Studies of Hyslop, Palmes, Alford, Monaco, and Fairhall (*2526*) 1943 indicate that no particular toxicity can be established for beryllium itself. It appears that the toxicity of beryllium salts is due to the toxicity of the acid radical such as the fluoride or the oxyfluoride, or to some objectionable condition brought about by the hydrolysis of certain of its salts, such as the chloride and the sulfate. Hyslop and his co-workers carried out animal experiments in which a number of beryllium compounds were injected intraperitoneally into guinea pigs at various concentrations. Beryllium compounds were also administered orally to young rats and guinea pigs, and, in addition, guinea pigs were exposed to the dust of beryllium compounds in high concentrations and over long intervals of time. These experiments gave no indication that beryllium is inherently toxic. Exposure of both guinea pigs and rats to the fumes arising from the electrolysis of molten fluorides containing beryllium fluoride or oxyfluoride indicated that these fumes are decidely toxic. In the authors' experiments, exposure to large amounts of beryllium by mouth, by inhalation, or by intraperitoneal injection resulted in very little storage of beryllium in the body. More beryllium was found to be stored in the liver than in the kidneys, and still more beryllium was found in the bone tissue. No significant changes in hemoglobin values were obtained, nor was there any evidence of polycythemia, or any other blood dyscrasia. Certain salts of beryllium, such as the fluoride and the sulfate, hydrolyze readily and these were found to have an irritant effect upon the skin, but this effect was absent in the case of the neutral salts. Recovery experiments indicated that absorption of beryllium from the alimentary tract is slight and that beryllium is excreted mainly in the feces. The absorption of beryllium carbonate from the lungs was also found to be very slight.

A comparison of the relative toxicities of beryllium, magnesium, and zinc by intraperitoneal injec-

tion revealed beryllium to be the least toxic and zinc the most toxic. Microscopic examination of the tissues of animals that had been exposed to beryllium by inhalation of beryllium dust or fumes, injection of beryllium compounds, or the oral administration of this material, indicated no specific relationship between beryllium and rickets, and no consistent pathological change which could be attributed to beryllium. The authors therefore concluded that since no particular toxicity could be established for beryllium, no safe permissible working standards should be based upon beryllium itself. Safe operating conditions must therefore depend upon other considerations than an implied toxicity of beryllium.

In initial studies of the inhalation toxicity of beryllium sulfate, Sprague, Pettengill, and Stockinger (*2533*) 1948 collected data from 66 animals representing 6 species on the toxic effects caused by inhalation of beryllium sulfate tetrahydrate at a concentration approximating 90 micrograms of the salt per cubic meter of air. The animals were exposed for 6 hours daily for a 2-week period in a small inhalation exposure chamber. The mortality for all species was 43 percent of the exposed animals. Weight response data showed that all species except the guinea pig were adversely affected by the exposure. The rat and the hamster revealed the greatest weight depression, losing 11 percent of their original weight. There was indication of renal impairment, with some subsequent regeneration in the rabbits. Much less serious kidney damage and hepatic injury in the dogs was indicated. The study showed an upward trend in the leukocyte count during the second week of exposure. The symptoms differed in each species. Ocular opacity developed in the dog, mouse, and guinea pig, whereas the rat developed rales. Other species were unaffected externally. Pulmonary edema was found in the mouse, rabbit, and rat. Hepatic injury was seen in mice dying during the first 9 days, not thereafter. Renal changes were seen in the rabbit and the rat, with some regeneration of the tubular epithelium in the former species. The authors believed that the sulfate ion contributed significantly to the toxicity of this beryllium salt.

LaBelle, Morrow, Booth, Wescott, and Melville (*2527*) 1949 have reported a study of beryllium poisoning on 325 rats and 18 rabbits, plus a smaller number of mice, guinea pigs, monkeys, and dogs receiving beryllium by intratracheal injection, usually as an insoluble compound, at levels ranging from 5 to 100 micrograms of beryllium per kilogram of body weight. In studies covering a period of 1 year after the injection, it was found that the chronic type of lesion developed in the lungs of most of the exposed animals. The characteristics of the lung lesions were specific within a given species and for a given compound, but were in no case identical with the human chronic pulmonary lesions. During the year's period most of the commonly measured variables in the blood and serum remained normal. The outstanding changes were increases in the blood platelets and the absolute polymorphonuclear leukocyte content of the circulating blood. In a study on the mechanism of action of beryllium, DuBois, Doull, and Cochran (*2517*) 1949 observed the acute effect of beryllium chloride upon carbohydrate metabolism and on various enzymatic reactions. Aqueous solutions of beryllium chloride were administered intraperitoneally to rats and the LD–50 value was found to be 0.6 milligram of beryllium per kilogram of body weight. Following acutely toxic doses of beryllium, there was a striking hyperglycemia. This hyperglycemia could be prevented by insulin, ergotamine, or removal of the adrenal medulla, suggesting that the effect was induced by epinephrine. Five hours after administration of 7.5 milligrams of beryllium salts per kilogram of body weight, there was a 50-percent decrease in liver glycogen, and 48 hours after this dose of beryllium there was a depletion of phosphocreatine and a striking increase in inorganic phosphorus in the liver. High concentrations of beryllium did not inhibit the oxidation of glucose or anaerobic glycolysis. Alkaline phosphatases activated by calcium or magnesium were strongly inhibited by beryllium.

Caccuri (*2514*) 1941 has reported alteration of the liver and the kidneys in beryllium poisoning. Daily doses of 1 milligram per kilogram body weight of beryllium (as carbonate, nitrate or oxide) were injected into rabbits and the animals were sacrificed 30 to 90 days later. At the end of 1 month, the liver and kidneys were still normal, but there was a slight hyperglycemia in all animals given the nitrate. There was venous congestion of the liver and sometimes venous dilatation. At the end of 2 months, this congestion became more pronounced in both the liver and the kidneys, and the former began to show fatty degeneration. The renal tubules were enlarged and filled with proteinaceous material. The author concluded that the nitrate is the most toxic beryllium compound of those used in the experiments reported.

Regarding the diagnosis of acute or chronic berylliosis, Dutra, Chalak, and Hubbard (*2519*) 1949 have reported that in some cases the diagnosis may be supported by the analysis of the urine for beryllium. In their study, beryllium was isolated

from the urine of persons working in beryllium plants who had no symptoms of berylliosis, although some had previously had the acute pulmonary condition. During acute or chronic berylliosis, the beryllium urinary excretion varies from day to day so that a few negative results do not exclude the diagnosis and an occasional case may never excrete beryllium in the urine. Appreciable amounts of beryllium were recovered from the lungs of all patients dead from berylliosis, except in one chronic case of nonoccupational origin. In some cases, beryllium was also recovered from other tissues.

As Vorwald has stated (*2537*) 1948, the pathological manifestations of the disease seen in beryllium workers are observed principally in the lungs and the tracheobronchial lymph nodes. Two distinct types of changes are recognized: (1) the acute form which resembles a pneumonic process and is attended by edema, hemorrhage, and exudate, but without the polymorphonuclear leukocytic responses that accompanies an acute infectious process, and (2) the chronic form characterized by a diffuse pulmonary reaction and scattered granulomatous lesions throughout both lungs. Dutra (*2518*) 1948 described a boggy, generalized consolidation of both lungs in the acute pneumonitis which simulates to some extent the stage of gray hepatization in lobar pneumania. Microscopically, in the acute form there is a diffuse intraalveolar exudate composed of large mononuclear phagocytes and edema fluid. In the chronic condition, the lungs are voluminous and emphysematous. Enlargement of the right ventricle of the heart is constantly present.

Cases of acute pneumonitis in workers exposed to beryllium oxide and metallic beryllium have been reported by Aub and Grier (*2511*) 1949. These cases indicate to the authors that the beryllium ion is toxic in its own right, and that the effects of exposure are not always attributable to the acid radicals of soluble beryllium salt. For information on acute dermatitis and pneumonitis in beryllium workers, the reader is referred to a review of 406 cases in a 6-year period reported by DeNardi, Van Ordstrand, and Carmody (*2516*) 1949. The report concerns acute dermatological and respiratory tract manifestations of beryllium poisoning encountered in three plants in the Cleveland area. More than 25 percent of the new employees in contact with beryllium inorganic salt fumes and dusts suffered skin reactions within 10 days after exposure. A serious problem was the development of acute beryllium ulcers of the skin which sometimes became chronic. These ulcers result from a deposition of minute beryllium sulfate tetrahydrate crystals in the skin through abrasion portals. Treatment consists of an incision of the papule, removal of the crystals in the acute ulcers, and curettage of the fibrous base in both the acute and chronic phases. The incidence and mortality of pneumonitis, the severest form of the respiratory tract disorders arising from the beryllium contamination, are the cause of concern. The irritative phenomena present in these cases are stated by the author to be the result of reactions in the bronchioles to some inorganic salts of beryllium or histaminelike byproducts, which cause spasm and partial blocking of the finer respiratory passages. There is interference with gas exchange in the alveoli, resulting in local anoxia, a colloidal imbalance, and in alveolar edema. The intermittant use of oxygen and hospitalization are recommended.

Serious, acute pulmonary changes resulting from beryllium sodium fluoride dusts in experimental animals have been reported by Policard (*2530* and *2542*) 1948. In these experiments, there is early and violent pulmonary edema with death of the animals within 24 hours. Beryllium oxide dusts, on the other hand, result in hyperplasia of the mesenchyma of the lung. Three types of reaction were reported, the first being a histiocyte pneumonia; the second, granulomatous nodules, often with giant-cell formation; and the third, thickening of the alveolar walls. The granulamatous nodules were seen after a few weeks of exposure and persisted for several months. In Policard's experiments, metallic beryllium and beryl did not seem to affect the lungs of the experimental animals. Carriere, Fraisse, Richard, and Roche (*2515*) 1949 and Wilson (*2539*) 1948 have described cases of delayed chemical pneumonitis or diffuse granulamatosis of the lung due to beryllium inhalation. These cases were all characterized by a delayed onset and somewhat chronic course. Carriere and his coworkers describe symptoms including irritation of the eyes, nose and air passages, varying in intensity with individual cases. The ocular and nasal irritation subsided in several days or a few weeks, but then the cough and dyspnea appeared to get worse, keeping the patients from work. The dyspnea followed effort and sometimes drifted into asthmatic attacks occurring frequently at night. Symptoms gradually disappeared, leaving behind a sensitivity of the air passages to vapors or fumes. In 1 or 2 cases, the X-ray showed shadows indicative of some discrete reticulonodular lesions, which in their turn tended to disappear in time. The distinctive features of these cases are the short exposure, the delayed onset of severe pulmonary symptoms, and final complete recovery after several months. For further reports of respiratory

tract involvement in beryllium poisoning, papers by Hardy and Tabershaw (*2524*) 1946; Pascucci (*2529*) 1948; Van Ordstrand, Hughes, and Carmody (*2535*) 1943; Van Ordstrand, Hughes, DeNardi, and Carmody (*2536*) 1945 may be consulted.

Reference may be made to experimental beryllium rickets reported in 1931 by Branion, Guyatt, and Kay (*2512*). These authors found that by replacing the calcium carbonate in Steenbock's rachitogenic ration 2965 with an equivalent amount of beryllium carbonate, bone lesions were produced in young rats which were similar to rickets. These changes were brought about by quantities of beryllium as low as 1 percent of the diet. Both the X-rays and histological sections revealed an almost complete failure of calcium deposition immediately proximal to the epiphyseal disc of the long bones. The onset of this type of rickets was not found to be preventable by cod-liver oil or irradiated ergosterol, both in generous quantities, or by irradiation with ultraviolet light. In 1949, Branion, Tisdall, and Drake (*2513*) reported that while the addition of 0.5 percent beryllium carbonate to the ration had little or no effect on long bone formation in the chick, nevertheless the addition of 1 to 2 percent beryllium carbonate resulted in beryllium rickets, characterized by low levels of inorganic plasma phosphorus, subnormal percentage of ash in leg bones, and failure in calcification and bone development. It was found that chickens were more resistant to beryllium rickets than were rats.

Pathological pulmonary changes in 12 chronic cases that came to autopsy have been reported by Gardner (*2521*) 1946. In these cases there were minute compact granulomatous nodules barely visible to the naked eye, distributed more or less uniformly within the walls of the airspaces throughout both lungs. In a case reported in England in 1948 (*2540* and *2541*), death was due to granulomatous fibrosis of the lungs and failure of a hypertrophied right heart. Microscopically, the lungs resembled silicosis and sarcoidosis, but were not typical of either of these. The patient in question was a 36-year-old physicist who had been working with beryllium oxide from December 1941 to December 1942 in connection with research on fluorescent lamps. He remained apparently well until 1945. The patient then began to complain of cough, breathlessness, and great loss of weight. He was eventually admitted to the London Hospital, where he died on 4 November 1945. Autopsy showed that death was due to beryllium poisoning. Gardner (*2521*) has also emphasized the chronicity and the high mortality rate which characterize beryllium poisoning. He points out that the patients suffering from this condition have lived from 6 months to 4 years, finally dying with cachexia, progressive dyspnea, and heart failure. The onset of the disease may be delayed as long as 3 or 4 years after apparent cessation of exposure.

Although the characteristic pulmonary changes seen in human cases of chronic beryllium poisoning have not been reproduced exactly in animals under experimental conditions, nevertheless definite pathological changes have been observed in animals, and for such a study of the effects of inhalation of beryllium dust in guinea pigs, the reader is referred to a report by Fabroni (*2520*) 1935. A report by Shilen, Galloway, and Mellor (*2532*) 1944 on the health hazards in a plant manufacturing alloys of beryllium should be consulted.

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2513. Branion, H. D., F. F. Tisdall, and T. G. H. Drake. Beryllium rickets in chickens. *Chem. Abstr.*, 1949, *33:* 2946.

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4. CADMIUM

For information on the general subject of cadmium poisoning, papers by Hamilton and Hardy (*2543*) 1949, Johnstone (*2545*) 1948, Ross (*2547*) 1944, and the U. S. National Institute of Health (*2549*) 1942 should be consulted. Cadmium has probably more lethal potentialities than any other of the metals which may cause acute or chronic illness. It has for a long time been a rare metal in industry, but has now become widely used in the manufacture of alloys and for electroplating. Cadmium is extracted from zinc ores as a condensation product. It is also found in the sludge after the electrolytic recovery of zinc. Cadmium is used in making storage batteries, in metal bearings, ceramics, cadmium vapor lamps, and in rustproofing. Cadmium poisoning usually occurs from the accidental absorption of cadmium fumes or dusts through the respiratory system, seldom by ingestion. The maximum allowable concentration of cadmium dust or fumes is given by Jacobs (*2544*) 1949 as 0.1 mg. per cu. mm. of air.

The lungs bear the brunt in all cases of cadmium fume inhalation. The first symptoms are usually smarting of the eyes and dryness and irritation of the throat. This is followed by severe, constricting pain in the chest and marked dyspnea. There may be coughing and a feeling of prostration, and sometimes giddiness and headaches. Three or four hours after exposure, the respiratory distress becomes increased in severity and gastric disturbances make themselves manifest with nausea, retching, vomiting, and occasionally diarrhea. There is frequently pyrexia with rigors and striking prostration. In the event of prolonged exposure to cadmium, pneumonia may supervene, and in fatal cases there may be signs of kidney and liver involvement. In moderate cases of cadmium intoxication, the patient is pale, dyspneic, prostrated, inclined to retch, and the pulse rate and temperature rise. The serious case shows evidence of diffuse bronchopneumonia, best revealed by X-ray. Ross (*2547*) has reported 23 cases of cadmium poisoning with no fatalities. Osol, Farrar, Leuallen, Verwey, Youngken, Detwiler, and Wood (*2546*) 1947 have pointed out that death may occur after the fifth or seventh day. They call attention to the fact that acid foods dissolve cadmium from metal containers containing this element. A concentration of only 30 p. p. m. of cadmium in solution causes, within 10 to 30 minutes, nausea, vomiting, abdominal cramps, weakness, and diarrhea, with recovery usually in 5 or 6 hours after this amount of cadmium ingestion. In a fatal case of cadmium poisoning described in 1943 in the Journal of the American Medical Association (*2550*), a worker died within 4 days after a prolonged exposure to a high concentration of cadmium fumes in an Indiana plant. The deceased worker undertook a job of "flanging" a cadmium-plated, stainless-steel pipe. To produce the flange, the pipe was heated with a blowtorch until it became cherry red. Soon

after beginning the operation, employees complained of irritation of the nose and throat as well as the thick blue smoke present in the environment. Within 4 hours, 2 employees became violently ill and were taken home. Vomiting, chest pains, and shortness of breath were the chief symptoms at this time. The chest symptoms of one worker increased, and within 4 days this man died. Four case histories are described by Johnstone (*2545*), who also has discussed treatment, recommending the immediate use of an oxygen tent for relief of air hunger. A method for the microscopic detection of cadmium oxide particles in lung tissue of experimental animals is described by Thiers, Arthur, Mills, Hamly, and Beamish (*2548*) 1947.

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5. CHLORINE

Chlorine gas is a powerful lung irritant, and was the first chemical war gas used in World War I. In the past, chlorine has been liberated in submarine compartments through leakage of salt water into the storage batteries. Victims of inhaled chlorine gas show dyspnea, cyanosis, and coma. There is a sense of suffocation, constriction in the chest, and tightness in the throat, and death may ensue if resuscitation procedures are not promptly carried out. The patient is likely to recover if immediately removed to fresh air. There may be areas of sloughing of the mucous membranes of the nose, throat, or bronchi. If the gas is swallowed, there may be necrosis of the mucosa of the esophagus or stomach. Marked irritation of the conjuntivae is also a characteristic feature. Nearly all cases of chlorine poisoning tend to recover completely if the victims survive the first 24 hours. Secondary infection of mucous surfaces is a possible complication. Reed and Harcourt (*2563*) 1941 believe that chronic exposure to chlorine gas does not result in real occupational disease so far as serious disability is concerned. The inhalation of small concentrations of chlorine over long periods of time may cause dental caries, acneform dermatitis, and chronic bronchitis. For reports on maximum allowable concentrations of chlorine gas in the environment, the reader is referred to papers by Fairhall (*2554*) 1949, Heyroth (*2556*) 1948, Jacobs (*2558*) 1949, and Skljanskaja and Rappoport (*2565*) 1934–35. Fairhall (*2554*) has pointed out that concentrations of chlorine of 40 to 60 p.p.m leads to pneumonitis and edema of the lungs. It is stated that 30.2 p.p.m. cause coughing, and with 3.5 p.p.m. there is a detectable odor of chlorine. The maximum allowable concentration is described as 0.35 to 4.0 p.p.m. for exposures of one-half to 1 hour. Skljanskaja and Rappoport (*2565*) have observed catarrh-like changes in the upper respiratory tract with hemorrhage and emphysema in the lungs of rabbits exposed to a chlorine concentration of 0.7 to 1.7 p.p.m., and these authors assert that chlorine appears to sensitize the respiratory tract to infection. Heyroth (*2556*) has stated that 1,000 p.p.m. is a fatal concentration for even large laboratory animals. If death does not occur, there may be pulmonary edema. The conjunctivae become inflamed and there is coughing and dyspnea. The respiratory rate of experimental animals subjected to this concentration of chlorine becomes increased during exposure. When the concentration is 1,000 or more p.p.m., inspiration becomes slower and deeper. The author has stated that men may work without interruption in air with 0.003 to 0.006 mg. of chlorine per liter. Exposures to low concentrations of 0.01 to 0.02 mg. per liter or 3 to 6 p.p.m. cause stinging and burning of the eyes, nose, and throat, and sometimes headache. There may be redness and watering of the eyes, sneezing, coughing, and laryngitis. Bleeding of the nose may occur and the sputum may be bloodtinged. Exposure for one-half to 1 hour to 0.04 to 0.06 mg. per liter, that is to say, 14 to 21 p.p.m., is dangerous and a concentration of 0.29 mg. per liter, that is to say, 100 p.p.m., cannot readily be borne longer than 1 minute. Dangers of low concentrations are limited to the nose and throat because of the solubility of chlorine in water. Higher concentrations give rise to pulmonary congestion and edema, the seriousness of which is increased by bronchoconstriction. Heyroth has pointed out that men lose their ability to detect chlorine in small concentrations. He also

states that workers exposed in bleaching rooms to concentrations of 0.015 mg. per liter, that is to say, 5 p.p.m., suffer from bronchial diseases and tend to be predisposed to tuberculosis. The teeth become corroded, and ulceration of the mucous membrane of the nose occurs.

Many experimental studies of the toxicity of chlorine were carried out during and immediately following World War I. Two such investigations are reported by Barbour (*2551*) 1919–20 and Klotz (*2559*) 1917. Barbour called attention to the effect of chlorine in concentrations of 20 to 30 p.p.m. of air in producing considerable increase in the body temperature of dogs. He stated that dogs gassed with lethal concentrations of chlorine tend to become poikilothermous, that is to say, they lose their capacity to regulate body temperature in environmental extremes. Barbour considered that peripheral nerve irritation produced by chlorine exerts inhibitory effects upon the temperature centers of the nervous system and may thus contribute substantially to the derangement of the heat-regulating mechanism seen with the concentrations of chlorine employed in his experiments. On the basis of his studies, he recommended that, in the treatment of gassed cases, an excessively warm environment may be as dangerous as one which is too cold. A further paper on the toxic effects of chlorine upon the lungs is that published by Barbour and Williams in 1919–20 (*2552*).

For descriptions of clinical cases of chlorine poisoning, papers by Doub (*2553*) 1933; Olliver and Charpin (*2561*) 1947; and Smith, Chassis, Bannon, Helm, and McLeod (*2566*) 1944 may be consulted. The latter gives an account of the well-known Brooklyn chlorine accident. On 1 June 1944, a truck carrying 27 cylinders of chlorine from Bayonne, N. J., to Brooklyn, N. Y., was found to contain a leaky cylinder. When the driver discovered the leak, he came to a stop approximately 30 feet from a subway entrance and 18 inches from a series of gratings covering ventilation shafts leading from the sidewalk to the subway station platform. Liquid chlorine spilled into the gutter adjacent to the gratings. Sufficient chlorine gas entered the station to cause a number of passengers to leave the train and go to the street. Some left the train at the next stop to obtain medical aid. There were 104 cases of chlorine poisoning, and 102 of these were from the subway. A total of 418 persons exposed were examined at 8 hospitals. Two hundred and eight were admitted for observation. Thirty-three victims were hospitalized for 1 to 2 weeks. The symptoms occurring after the first few hours after exposure consisted of burning of the eyes, nose, and mouth, with increased salivation, cough, choking sensation, and substernal pain accompanied by nausea, vomiting, headache, and dizziness. There was syncope in 8 out of the 33 cases. Six to ten hours after exposure, the casualties were perturbed and acutely ill, and suffered from moderate to severe respiratory distress. Cyanosis of the mucous membranes was frequent. The respiratory rate was increased and was costoabdominal in type. Dry and moist rales were a universal finding. Symptoms tended to subside within 24 hours. Oxygen was given to all acutely ill victims over a period of 96 hours, and pressure breathing in 20 cases reduced respiratory distress and resulted in the disappearance of pulmonary sounds. Bronchodilating drugs, such as epinephrine and aminophyllin, were stated to be beneficial.

The reader is referred to a report on respiratory studies made during the late stages of gas poisoning by Pearce (*2562*) 1920. This author found that the majority of men complained of symptoms which they believed to be due to gas fail to show any signs of cardiac or pulmonary impairment. These patients suffered from subjective symptoms similar to those of the so-called effort syndrome. One patient who had been gassed with chlorine 1 year previously showed no cardiovascular or pulmonary impairment, save some bronchitis. He complained of inability to work without becoming restless and faint.

Treatment of chlorine gas poisoning includes early administration of oxygen. Oxygen treatment for chlorine-gas exposure has been described by Nale (*2560*) 1946. On experimental grounds, Hjort and Taylor (*2557*) 1919 concluded that the administration of morphine exerts, if anything, an unfavorable influence upon the ultimate outcome of chlorine poisoning. They reported that in dogs gassed with chlorine, the administration of morphine in 10 mg. per kilo body weight doses may temporarily prolong the maintenance of a high alkali reserve level and so tend to counteract a rapidly advancing acidosis produced by chlorine gas inhalation. The bronchoconstriction resulting from inhalation of chlorine gas has been studied by Gunn (*2555*) 1919–20. The author concluded that the immediate bronchoconstriction is produced reflexly by the first contact of the irritant chlorine vapor with the bronchial mucous membrane. Continued inhalation of the gas produces thereafter an apparent slight and gradual bronchoconstriction, but from histological observation it appeared to the author that this is due rather to edema of the bronchial mucous membrane than to contraction of the bronchial muscle. In Gunn's experiments, a num-

ber of bronchodilator drugs were investigated, and it was concluded that, for practical purposes, atropine or epinephrine might be the most useful.

For experimental investigations of the pathological changes resulting in animals from exposure to chlorine gas, papers by Klotz (*2559*) 1917; Schultz and Hunt (*2564*) 1918; and Weedon, Hartzell, and Setterstrom (*2567*) 1940 may be consulted. Weedon, Hartzell, and Setterstrom (*2567*) exposed rats and mice to various concentrations of chlorine from 63 p.p.m. to 1,000 p.p.m. With the highest concentrations, the brain was congested. The lungs were distended, pale, and waxy, and the cut surfaces foamy. The right heart was greatly distended, the liver was congested, the stomach moderately to greatly distended, and there was distention of the intestines and congestion of the kidney. Klotz (*2559*) found that the acute reaction in the lungs of animals exposed to chlorine was mainly an intense congestion with edema and capillary thrombosis. Animals surviving for a longer period exhibited pulmonary infiltration of inflammatory cells, mainly lymphocytes. The acute capillary thrombosis appears of importance in acute death when the concentration of chlorine is great. There is a tendency toward increased viscosity of the blood, and this, together with capillary thrombosis, impedes the ready flow of blood through the lungs and leads to a fall in systematic arterial blood pressure. Post-mortem study of the lungs of cats and dogs exposed to chlorine gas by Schultz and Hunt (*2564*) revealed varying degrees of edema together with separation of the epithelium from wide areas of the respiratory tract. The alveoli and the finer air passages were invaded by serous exudate.

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2554. Fairhall, L. T. Chlorine. pp. 51–53 in: *Industrial toxicology.* Baltimore, The Williams & Wilkins Co., 1949, 471 pp.

2555. Gunn, J. A. The action of chlorine, etc., on the bronchi. Report to the chemical warfare committee. *Quart. J. Med.,* 1919/1920, *13:* 121–127.

2556. Heyroth, F. F. Chlorine. pp. 545–549 in: *Industrial hygiene and toxicology.* Edited by Frank A. Patty. New York, Interscience Publishers, Inc., 1948, 1138 pp.

2557. Hjort, A. M. and F. A. Taylor. The effect of morphine upon the alkali reserve of the blood of dogs gassed with fatal concentrations of chlorine. *J. Pharmacol.,* 1919, *13:* 407–416. [P]

2558. Jacobs, M. B. Common poisonous compounds of the halogens. A. Chlorine. pp. 373–390 in: *The analytical chemistry of industrial poisons, hazards, and solvents.* Second edition. New York, Interscience Publishers, Inc., 1949, 788 pp.

2559. Klotz, O. Acute death from chlorine poisoning. *J. Lab. clin. Med.,* 1917, *2:* 889–895.

2560. Nale, T. W. Oxygen treatment for chlorine gas exposures. *W. Va. med. J.,* 1946, *42:* 178–180.

2561. Ollivier, H. and J. Charpin. A propos d'une intoxication accidentelle collective par le chlore. *Ann. Méd. lég.,* 1947, *27:* 150–151. [CH]

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2566. Smith, H. W., H. Chassis, J. H. Bannon, J. Helm, and C. M. McLeod. Brooklyn chlorine accident. A technical and medical report. U. S. Army. Chemical warfare service, Medical division. *Contract W–49–036–csw–1* with New York University, College of Medicine. 1 July 1944, 36 pp. xci. [CH]

2567. Weedon, F. R., A. Hartzell, and C. Setterstrom. Toxicity of ammonia, chlorine, hydrogen cyanide, hydrogen sulphide, and sulphur dioxide gases. V. Animals. *Contr. Boyce Thompson Inst.,* 1940, *11:* 365–384. [P]

6. LEAD

Brown (*2572*) has reported that the incidence of lead poisoning among U. S. Navy personnel decreased between 1922 and 1944. Two factors responsible for this reduction in incidence were the changes in 1931 from a paint containing 70 percent red lead to one containing only 29.5 percent and the changeover to zinc chromate paint in 1941. Probably improvements in hygienic control were of even greater importance. So far as can be ascertained, shipbreaking during the 2 years immediately following World War II produced very few cases of plumbism, a condition very common in this occupation after World War I. The route by which lead enters the organism most rapidly is the respiratory tract, and lead absorbed by this route produces the most serious symptoms. Next in danger comes the continued ingestion of lead compounds by mouth, and least harmful of all the possible routes is a slow cutaneous absorption in persons with broken or irritated skin. Lead compounds may reach the mouth via contaminated hands, or lead fumes may be inhaled during grinding or filing, during painting with lead paints, or cutting, burning, or chipping of lead painted surfaces. The upper limit of safety

for industrial lead exposure has been given by Kehoe (*2583*) 1948 as 1.5 mg. per 10 cubic meters of air. The upper limit of safe urinary excretion of lead does not exceed 0.15 mg. per liter of urine. Kehoe (*2582*) indicated that the safe level for the ingestion of lead in food and drink is greater than 0.3 mg. and less than 0.6 mg. per day. It is significant physiologically that from 95 to 98 percent of lead present in the body in lead poisoning is found in the erythrocytes in the blood. Only a small quantity of the lead ingested is absorbed into the body. The absorbed portion is distributed to the tissues, including the liver, from which it is partially secreted back into the alimentary tract with the bile. This action of the liver in withdrawing lead from the body and secreting it into the alimentary tract is responsible for the fact that the ingestion of lead is less dangerous than its inhalation. Lead poisoning is stated by Jacobs (*2580*) 1949 as 10 times more likely to occur through inhalation than by ingestion. The toxicity of lead depends upon a number of factors—its solubility in body fluids; the length of time in contact with the body fluids; the quantity ingested, inhaled, or absorbed; and the quantity in the circulation at a given time. Inhalation of 1.45 mg. of lead per day is stated by Jacobs to produce lead poisoning within 2½ years. Hamilton and Hardy (*2578*) 1949 have pointed out that various compounds of lead differ in their toxicity. Metallic lead particles in the lung act much as do silica particles, setting up a fibrotic process, which paves the way for a pulmonary tuberculosis. Absorption by the respiratory tract is extremely rapid. Skin absorption is slight, except in the case of tetraethyl lead. Absorption of lead by the alimentary tract is minimized by excess of phosphate ions which keep the lead insoluble. Lead is carried in the blood as the dibasic phosphate or as the glycerophosphate, and is deposited in the skeleton as the very slightly soluble tribasic phosphate. The liver, spleen, lungs, and kidneys may retain lead for a short period, during which the excretion rate is highest (a few weeks). Redistribution of lead results in a shift of most of the remaining amount to the bony skeleton with small amounts retained in the liver and spleen.

The most consistently harmful effect of abnormal lead absorption is on the blood cells. Anemia is invariably present. Basophilic stippling is always seen in the acute stage of lead intoxication, but is not pathognomonic of plumbism since basophilic stippling may be present in other diseases of the blood. The mechanism of intestinal colic in lead poisoning is not clearly understood. Usually other symptoms precede the colic. The gastrointestinal symptoms usually begin with anorexia, disagreeable sweetish taste in the mouth, dyspepsia, and obstinate constipation. There is also lassitude and malaise with pain around the umbilicus, and spasmodic contraction of the abdominal wall. The colic is typically decreased by pressure, and there is no tenderness. This colic has been ascribed by some authors to vagal irritation produced by the lead. A characteristic phenomenon is wrist drop due to paralysis of the extensor muscles of the forearm. There may be considerable wasting of the muscles. The lead line may be present, a bluish black stippling along the lower incisors at the gum margin.

The reader is referred to several comprehensive treatises on lead poisoning. These include monographs or articles by Aub, Fairhall, Minot, and Reznikoff (*2568*) 1925, Cantarow and Trumper (*2573*) 1944, Hamilton and Hardy (*2578*) 1949, and Johnstone (*2581*) 1948. The review by Aub and coworkers contains an excellent bibliography of 500 references. Papers by Brandt and Reichenbach (*2571*) 1943 and Heyroth (*2579*) 1948 may also be consulted. Fine (*2576*) 1923–24 has indicated that metallic lead is less readily phagocytosed than is basic lead carbonate. The presence of soluble lead impairs the phagocytic properties of the leukocyte, and in the presence of metallic lead the phagocytosis of carbonate is retarded. The rate of phagocytosis of metallic lead by leukocytes is of the same low order of magnitude as that of quartz. These facts suggest to the author that metallic lead, like quartz, remains as a foreign body in the lung and excites fibrosis.

Regarding the absorption and excretion of lead under normal conditions and in lead poisoning, the reader is referred to papers by Cholak and Bambach (*2574*) 1943 and Kehoe, Thamann, and Cholak (*2584, 2585*) 1933. The latter authors point out that the normal adult American excretes lead at a rate of 0.02 to 0.08 mg. per liter of urine and at a rate of 0.03 to 0.1 mg. per gram of ash in the feces. The mean daily individual output of lead for various groups of normal persons varies from 0.25 to 0.38 mg. The lead intake in food of selected normal subjects is approximately equivalent to the lead content of their feces, and this may be taken as evidence, not only of the passage of the great proportion of the ingested lead through the alimentary tract unabsorbed, but also of the predominant source of the lead which is absorbed and excreted by normal persons. It is calculated from direct analytical observations on food and from indirect interpretation of the fecal lead content of a large group of normal subjects that the daily intake of lead in the food is normally of the order of 0.16 to

0.28 mg. Normal persons whose lead metabolism is followed for prolonged periods show no evidence of lead accumulation, but appear to have established an equilibrium with their environment, in which the excretion of lead keeps pace with the absorption. Post-mortem analysis of the tissues of normal subjects indicates a total lead content in the adult body of 135 mg. Administration to a human subject of 1 mg. and 5 mg. of lead chloride daily for short periods resulted in the elimination of the greater portion of the lead unabsorbed, and in the absorption of amounts slightly less than 0.5 mg. daily for the former dosage and approximately 1 mg. daily for the latter. These amounts of absorbed lead are sufficient to produce a measurable increase in the rate of urinary lead excretion during a period of active absorption and for a time thereafter. Persons who have absorbed abnormally large amounts of lead excrete lead at a higher than normal rate after the cessation of lead exposure. The duration of the period of increased lead excretion depends upon the extent of lead absorption. The rate of lead output diminishes rapidly for a period of several weeks, after which there is a prolonged and gradual diminution in excretory rate until the normal level is reached. The relative intensity of the lead exposure is indicated by the initial height of the excretory level, by the sharpness of the decline in the excretory rate during the early weeks of freedom from exposure, and by the duration of the period of high excretory rate. Persons abnormally exposed to lead show unusually large amounts of lead in their circulating blood during life, and in their tissues at necropsy for variable periods of time after the discontinuance of exposure. The total amount of lead in the body depends upon the severity of the lead exposure and the interval between exposure and death. The detection of an abnormally high rate of lead excretion or an unusual amount of lead in the tissues is useful in estimating the severity of the lead exposure. It does not constitute proof of the existence of lead intoxication.

Cholak and Bambach (*2574*) 1943 have reported normal lead concentrations in human subjects of 0.030 mg. per 100 grams of blood, 0.027 mg. per liter of urine, and 0.27 mg. per 24-hour fecal sample. Exposure in industry causes a definite increase in the mean lead concentration in proportion to the severity of exposure. The lead content of either the urine or the blood serves as a better criterion of lead exposure than the concentration in the feces. Analytical data from large representative groups of workmen may be set up in the form of histograms to determine the character of exposure in a plant. Distribution of results and mean values obtained over extended periods of time can be used as measures of the uniformity and efficacy of means employed to control lead exposure. For further reports on the subject of absorption and excretion as well as differential diagnosis of lead poisoning, papers by Aub, Minot, Fairhall, and Reznikoff (*2569*) 1924 and Belknap (*2570*) 1949 may be consulted.

For case histories of lead poisoning, the reader is referred to papers by Cotter (*2575*) 1946, Gent (*2577*) 1945, d'Onofrio (*2587*) 1950, and a paper in the Journal of Industrial Medicine (*2591*) 1947. Ten cases cited by Cotter (*2575*) were from a group of 30 workers who were demolishing an elevated railroad with blowtorches which involved cutting through layers of steel and paint. Unless positive pressure respirators were worn, the incidence of inhaled lead poisoning ran as high as 80 percent. Most of the patients had cramps, nausea, constipation, and abdominal tenderness, and showed a lead gumline. Some complained of muscular weakness. There was an elevation of the reticulocyte count in the blood and a lowering of granulocytes and hemoglobin. The blood cholesterol, nonprotein nitrogen, carbon dioxide content, phosphorus, and protein were all within normal limits. The lead content of the urine varied from 0 to 0.2 mg. per 100 cu. cm. A high lead content of the urine is usually considered unfavorable, but the author believed that in this series it indicated a high rate of elimination with a more favorable prognosis. Reference *2591* reports an unusual case of lead poisoning in a man who worked in a shooting gallery for 2 years. Air analysis in the shooting gallery showed toxic air concentrations of lead dust of 7 to 60 times the maximum allowable concentration. The source of lead in the air was from bullets hitting the targets.

As Wilentz (*2590*) 1949 has stated, treatment should be directed towards overcoming the intestinal colic, correcting the anemia, and restoring the patient to his job symptom free with no disability. Depending upon the severity of symptoms, hospitalization may be necessary in the acute stage. It is probable that the storage of lead may be minimized by keeping the bones filled with calcium by means of a high calcium diet. The colic may be relieved by antispasmodics, such as atropine, or by intravenous administration of calcium gluconate. Wilentz does not recommend the use of narcotics. Cases should be followed with complete blood cell count and stippling determination, also estimation of lead in the urine and a complete urinalysis. Wilentz does not recommend measures to hasten the excretion of lead from the body since this involves certain dangers, prolongs hospitalization

and disability, and because the results are considered uncertain. Calcium immobilization therapy is advocated because of its safety and simplicity and because of favorable results. Cotter (*2575*) also speaks favorably of the antispasmodic action of intravenous calcium gluconate. However, he points out that calcium gluconate is not a curative agent and that there is an attendant danger of renal calculi.

The use of sodium citrate has been recommended as a prophylactic or therapeutic procedure. Shiels, Thomas, and Palmer (*2589*) 1951 have recommended the administration of sodium citrate in oral doses of 4 or 5 grams in water once a day as a preventive procedure in employees exposed to lead. Evidence from a study of stippled cell counts and lymphocytes before and after commencing this prophylaxis suggests that sodium citrate is useful in preventing ill-effects of increased lead absorption. The authors are careful to point out that sodium citrate prophylaxis is not a substitute for improved working conditions, but is a useful adjunct. Kety and Letonoff (*2586*) 1943 have reported the results of sodium citrate therapy in 15 cases of lead poisoning in adults. Sodium citrate administration resulted in a significant fall in the blood lead concentration, and an early and persistent amelioration of the symptoms of lead poisoning. Intravenous administration of sodium citrate resulted in the immediate relief of severe colic in 2 of 4 patients presenting this symptom. There were no ill-effects of sodium citrate nor any recurrence of symptoms following therapy. For a further discussion of the treatment of lead poisoning, the reader is referred to an article by Osol, Farrar, Leuallen, Verwey, Youngken, Detweiler, and Wood (*2588*) 1947.

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2573. Cantarow, A. and M. Trumper. *Lead poisoning.* Baltimore, The Williams & Wilkins Co., 1944, 264 pp. [R]

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2578. Hamilton, A., and H. L. Hardy. Lead. pp. 49–103 in: *Industrial toxicology.* Second edition. New York, Paul B. Hoeber, Inc., 1949, 574 pp. [R]

2579. Heyroth, F. F. The metals (except lead). pp. 675–738 in: *Industrial hygiene and toxicology.* Edited by Frank A. Patty. New York, Interscience Publishers, Inc., 1948, 1138 pp. [R]

2580. Jacobs M. B. Lead, mercury, and arsenic. pp. 191–219 in: *The analytical chemistry of industrial poisons, hazards, and solvents.* Second edition. New York, Interscience Publishers, Inc., 1949, 788 pp.

2581. Johnstone, R. T. Lead. pp. 234–264 in: *Occupational medicine and industrial hygiene.* St. Louis, The C. V. Mosby Co., 1948, 604 pp. [CH]

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2583. Kehoe, R. A. Industrial lead poisoning. pp. 643–673 in: *Industrial hygiene and toxicology.* Edited by Frank A. Patty. New York, Interscience Publishers, Inc., 1948, 1138 pp. [R]

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7. MERCURY

Mercury poisoning is a potential hazard in any situation in which mercury vapor may be released into the air and taken in via the lungs. Under some circumstances mercury may also be ingested via contaminated hands. Beauchamp and Tebbens (*2592*) 1951 and Shepherd, Schuhmann, Flinn, Hough, and Neal (*2606*) 1941 have reported on the hazards of mercury vapor in university and other scientific laboratories. As Hamilton and Hardy (*2598*) 1949 have pointed out, mercury vaporizes even at the temperature at which water freezes.

Mercury may enter the body via the lungs, the alimentary tract, and the skin. Industrial mercurialism is characterized by three features: inflammation of the mouth, muscular tremors, and psychic irritability. According to Osol and coauthors (*2603*) 1947, the first signs of mild mercury poisoning are metallic taste in the mouth, slight soreness of the gums, and an unpleasant sensation in the sockets of the teeth when the jaws are firmly closed. Later the gums become swollen and a black line may be seen along the gingival margin. There is an increase in the quantity and viscidity of the saliva. The gums, tongue, throat, and face may all become swollen. The acute form of industrial mercurialism is largely a disease of the oral mucous membranes. The chronic intoxication is a disease primarily of the nervous system, and occurs from inhalation of metallic mercury vapor. Hazardous concentrations can result from seemingly negligible spillage of mercury, and probably as little as 1 part in 50 million parts of air is toxic in long air exposures. The acute effects are characterized by spongy gingivitis, anorexia, weakness, and dyspepsia. Following chronic exposure, there may be weight loss, pallor, and nervousness, plus a tremor which increases on the use of the limbs. There may be muscular pain with tension and cramps manifested at night. Dermographia, excessive perspiration, and blushing, together with exaggerated tendon reflexes, have also been observed. The nervous lesion is thought to be located in the basal ganglia, but the cerebral cortex may be the site of involvement. Advanced neurological defects due to mercurialism are extremely refractory to treatment. For further general studies of mercury poisoning, the reader is referred to articles by Fourcade (*2596*) 1950, Howard (*2600*) 1951, and Johnstone (*2601*) 1948. Reports by Fourcade (*2596*) and Hamilton and Hardy (*2598*) contain discussions of severe damage to the kidneys.

Nine cases of mercury poisoning from the use of antifouling plastic paint have been reported by Goldwater and Jeffers (*2597*) 1942. Plastic paint heated to a temperature of 350° F. prior to application was sprayed on ships at a Navy yard. Many men worked as long as 13 hours a day for several days at this operation. Toxic fumes containing mercury vapor were liberated during the heating and the spraying process. Men wearing gold rings observed a silvery coating of mercury amalgam on the rings. Personnel had been given charcoal respirators to wear, but were lax in the use of these protective devices. Among the 17 painters engaged in the operation, 9 developed illness diagnosed as mercury poisoning. Symptoms consisted of constipation, anorexia, nausea, vomiting, hoarseness, sore throat, tightness of the chest, sore gums, bad taste in the mouth, fatigue, nervousness, headache, dizziness, and bloody urine. There were tremors of the hands in five cases.

Turner (*2608*) 1924 reported that daily exposure to an atmosphere containing as small a quantity as 0.02 mg. of mercury per cubic foot of air results in signs and symptoms of poisoning. Clinical histories indicated that daily exposure must continue for 2 or 3 months, or more, before symptoms appear. It was estimated that in exposure to these quantities of mercury for 3 to 5 hours daily, there was a total daily absorption of mercury ranging from 0.771 to 1.285 mg., according to the duration of exposure. The author called attention to copper-colored discoloration of the mucous membrane of the pharynx, the pillars of the fauces, and the gums. This discoloration was constant in all cases, and the gums were swollen with enlargement of the capillaries. Superficial erosions appeared upon the mucous membrane of the gums and upon the buccal mucous membrane in the vicinity of the upper molar teeth. Perialveolar abscesses frequently occurred and caused considerable discomfort. Occasionally there was an appreciable increase in the flow of saliva. Urinalysis and differential blood counts showed the urine and the blood to be unaffected by the mercury absorbed. There was subjective tenderness of the gums and hypersensitiveness of the teeth, particularly those containing amalgam fillings. Intestinal peristalsis was slightly increased, occasionally developing into mild attacks of diarrhea. Shifting neuralgic pains were occasionally felt in various joints and in the chest.

Chronic mercurialism is a potential hazard in the hatters' fur-cutting industry and for reports of cases of mercury poisoning in this industry, papers by Neal, Jones, Bloomfield, and Dallavalle (*2602*) 1937 and Vigliani and Baldi (*2609*) 1948 may be consulted. The authors of the former paper stress the neurological and psychic disturbances. There may be tremor varying in degree from a slight tremor of the hand, eyelids, or tongue to marked, generalized tremor. Psychic imbalance may be present as indicated by irascible temper, discouragement without cause, feeling of depression or despondency, excessive embarrassment in the presence of strangers, timidity, desire for solitude, anxiety, excitability, inability to take orders, or a strong sense of self-consciousness. Christensen, Krogh, and Nielsen (*2595*) 1937 reported cases of acute mercury poisoning in a respiration chamber in personnel undergoing carbon dioxide experiments over a prolonged period. These subjects became ill with bronchial

irritation, violent coughing, and severe headache. After 3 days there was inflammation of the mouth. The cases were due apparently to spillage of metallic mercury. Cases of chronic mercury poisoning in a thermometer workshop have been described by Buckell, Hunter, Milton, and Perry (*2594*) 1946, and the reader is referred to a report on two deaths from exposure to the fumes of a diethyl mercury published in 1943 by Hill (*2599*).

Prophylaxis includes all of those procedures designed to prevent contamination of the environment with mercury. The treatment of contaminated surfaces such as floors is important. Renes and Seifert (*2604*) 1946 reported that the treatment of contaminated surfaces with polysulfides was not found to be an adequate control measure. Thorough washing of the contaminated surfaces followed by waxing was the most effective procedure for reducing the hazard of exposure. A brief report on prophylaxis by Sappington (*2605*) 1946 may be consulted. The reader may also consult papers by Brigatti and Baldi (*2593*) 1947 and Slutzky (*2607*) 1951.

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2596. Fourcade, J. Intoxications par le mercure et ses composés. pp. 117–126 in: *Médicine du travail.* Edited by C. Simonin. Paris, Librairie Maloine, 1950, 913 pp. [D]

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2598. Hamilton, A. and H. L. Hardy. Mercury poisoning. pp. 115–126 in: *Industrial toxicology.* Second edition. New York, Paul B. Hoeber, Inc., 1949, 574 pp.

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2601. Johnstone, R. T. Mercury, chromium, copper, and aluminum. pp. 310–316 in: *Occupational medicine and industrial hygiene.* St. Louis, The C. V. Mosby Co., 1948, 604 pp. [CH]

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2603. Osol, A., G. E. Farrar, E. E. Leuallen, W. F. Verwey, H. W. Youngken, D. K. Detweiler, and H. C. Wood, Jr. Mercury. pp. 690–692 in: *The dispensatory of the United States of America.* 24th edition, 1947. Philadelphia, J. B. Lippincott Co., 1928 pp.

2604. Renes, L. E. and H. E. Seifert. Mercury vapor hazards in certain chemical laboratories. *Amer. industr. Hyg. Ass. Quart.*, 1946, *7:* 21–25. [P]

2605. Sappington, C. O. Mercury exposures: evaluation and prophylaxis. *Amer. industr. Hyg. Ass. Quart.*, 1946, *7:* 26–28.

2606. Shepherd, M., S. Schuhmann, R. H. Flinn, J. W. Hough, and P. A. Neal. Hazard of mercury vapor in scientific laboratories. *J. Res. nat. Bur. Stands.*, 1941, *26:* 357–376.

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2608. Turner, J. A. Mercurial poisoning. A report on poisoning from small quantities of mercurial vapor. *Pub. Hlth. Rep., Wash.*, 1924, *39:* 329–341.

2609. Vigliani, E. C. and G. Baldi. An unusual outbreak of mercurialism in the felt-hat industry. *Proc. ninth intern. Congr. industr. Med., London,* 1948, 574–580. (French summary.)

8. STIBINE

Antimony hydride (SbH_3), known as antimoniuretted hydrogen and later as stibine, was discovered by Thomson working in England and independently by Pfaff in Germany in 1837. Both of these investigators were studying the Marsh test for arsenic.

Since battery grids often contain from 5 to 10 percent antimony, the production of stibine in perceptible quantities during overcharging of batteries is a potential hazard in submarines. That stibine is present in the air of submarines during battery-charging operations has been demonstrated by Webster, Liljegren, Fairhall, and Neal (*2614*) 1943. The stibine content of battery gas was investigated by these authors on five submarines under various operating conditions. Two regular charges, 2 equalizing charges, 1 equalizing charge followed by a rapid 6-hour discharge, and a normal discharge were studied. Chemical and spectrographic tests were carried out to establish the presence of antimony and/or arsenic compounds in battery gases. No stibine was detected during either the normal or rapid discharge of the batteries. However, stibine was regularly present during the latter part of the charging operations after gassing had begun. It was present when the hydrogen content amounted to 0.6 percent or more. When the battery gas was exhausted outboard via the main induction valve or via the vents in the conning tower, hardly a trace of stibine could be detected inside the boat. Under these circumstances, the stibine content was not more than 0.2 p. p. m. When the battery gas was discharged inboard, stibine could be quickly detected in various parts of the boat. A test carried

out on the U. S. S. *Paddle* showed an average of 0.6 p. p. m. during charging. From measurements made under usual dockside operating conditions, it is concluded that the concentration of stibine in the interior of a submarine is not likely to rise above a few tenths of a part per million unless the gas is exhausted inboard.

A major report on the toxicology of stibine appeared in 1951 under the authorship of Webster, Liljegren, Zimmer, and Dunn (*2617*). These studies were carried out on 775 animals of 9 species comprising mice, rats, guinea pigs, rabbits, cats, dogs, monkeys, frogs, and chicks. The animals received one or more exposures to stibine-air mixtures of known concentrations in order to study both the acute and chronic toxic effects. Concentrations of stibine from 9 p.p.m. to about 700 p.p.m. with durations of exposure varying between 4 minutes and one-half hour for a single exposure were used. The usual exposure period was 1 hour. These studies indicate that stibine is a highly toxic gas capable of inducing profound changes in the several experimental animals investigated. There is a wide species variation in susceptibility, dogs being most easily affected and the frogs the least. Stibine appears to act mainly as an irritant affecting primarily the deeper structures of the lung and with increasing concentrations and length of exposure producing pulmonary congestion followed by edema and even hemorrhages. With the lower concentrations, there is somtimes irritation of the nose and mouth, and watering of the eyes. There may be symptoms of shock such as hemoconcentration, asthenia, shallow rapid breathing, restlessness, reduced body temperature, and reduced peripherial circulation. Death may occur within 48 hours, and in most of these cases, fatality is due to involvement of the lungs and respiratory failure. In animals surviving for 48 hours, there may be secondary or delayed effects of stibine poisoning which may be fatal. In these delayed deaths the lethal action of stibine or its decomposition products is on the blood. The hemolytic action appears to vary not only with the concentration of stibine but also with the type of animal used. The red-cell count frequently increases immediately after exposure, suggesting hemoconcentration. The white-cell count usually drops immediately after exposure, and this is frequently followed the next day by leukocytosis. The red-cell count may fall for several days before the minimal value is reached. Providing sufficiently high concentrations of stibine are used, severe anemia may supervene as a result of a single exposure. In fatal cases, other complications such as severe liver damage are usually present. There may be hemoglobinuria; albuminuria is of frequent occurrence following the disappearance of hemoglobinuria. Sometimes bilirubin can be detected in the urine of animals, and urobilinogin regularly appears when severe liver damage occurs. The authors state that bile formation appears to be stimulated by the increased destruction of erythrocytes. However, bilirubin is hardly ever found in the plasma, since the animals are apparently able to excrete bilirubin rapidly via the liver. Consequently, frank jaundice was not seen in any of the species suffering from stibine poisoning with exception of the rabbits. In the dogs and the cats, there was vomiting, and in the rodents, diarrhea. At moderate to high concentrations of stibine, anoxia was commonly seen in all of the animals investigated, particularly the cats. There were other symptoms such as convulsions, exophthalmos, weakness of the hind quarters, and cyanosis.

With repeated exposures in the animal experiments, the authors found a successively lessened susceptibility to the action of stibine, and they attributed this to changes in the lung structure affecting the breathing pattern or to diminished breathing on successive exposures. In either case, less stibine would be inhaled as the exposures were repeated, and less marked effects would be expected. This apparent tolerance is lost on waiting several months between exposures and on raising the exposure level. The outstanding pathological findings revealed that autopsy include pulmonary involvement, congestion of the kidneys and spleen, fatty changes in the liver, and sometimes enlargement of the right heart. There are species differences in the toxicity of stibine which depend to some extent on body weight and activity. The smaller and more active animals appear to be more susceptible to the action of stibine. On the basis of these highly toxic effects of stibine on laboratory animals, the authors consider that stibine would probably be very toxic to man. Comparison of its toxicity with that of arsine using experimental animals suggested to the authors that the order of toxicity of arsine and stibine would be approximately the same for man.

Earlier reports by Webster, Liljegren, and Zimmer (*2615* and *2616*) 1944 and 1945 may be consulted. These reports include a description of methods of generating stibine. An outline of the rhodamine B method for the analysis of stibine content of air in chambers is given. For further studies on the methods of production and determination of small quantities of stibine, the reader may wish to consult papers by Rabideau and Thomas (*2611*) 1943 and Webster and Fairhall (*2613*) 1943.

Using radioactive antimony administered as stibine gas, Smith, Steele, Eakin, and Cowie (*2612*) 1948 measured the distribution of this substance in blood and tissues at successive time intervals following administration. The concentration of antimony in the blood stream exhibited a smoothly decaying curve, decreasing more rapidly in the guinea pig than in the chick. The red cells contained initially a much higher concentration of antimony than plasma, although the difference became reduced in time. The concentration curves in the lung, brain, muscles, and fat, were generally similar to those of blood. The curves for the liver and to a lesser extent the spleen, passed through a maximum about one hour following exposure. Approximately four hours after exposure, tissue antimony levels became constant; those for the liver, spleen, and kidneys were greater than for whole blood. All other tissues showed concentrations of antimony less than for blood, but were equal to or greater than the concentrations in plasma. The authors adduced evidence to show that the rate of elimination from the body is higher for the guinea pig than for the chick.

A chapter on stibine by Jacobs (*2610*) 1949 may be consulted.

2610. Jacobs, M. B. Stibine. pp. 259–261 in: *The analytical chemistry of industrial poisons, hazards, and solvents.* Second edition. New York, Interscience Publishers, Inc., 1949, 788 pp.

2611. Rabideau, S. W. and F. S. Thomas. A method of production and determination of small quantities of stibine. U. S. Navy. NRL. *No. P–2130, Rept. no. 3,* 3 August 1943, 6 pp.

2612. Smith, R. E., J. M. Steele, R. E. Eakin, and D. B. Cowie. The tissue distribution of radioantimony inhaled as a stibine. *J. Lab. clin. Med.,* 1948, *33:* 635–643. [P]

2613. Webster, S. H. and L. T. Fairhall. Progress report on the study of the toxicity of stibine. U. S. National Institutes of Health, Bethesda, Md. (*Coordinate Navy Project X–166, Rept. no. 2*), 26 July 1943, 3 pp.

2614. Webster, S. H., E. J. Liljegren, L. T. Fairhall, and P. A. Neal. Report on a field trip to the U. S. submarine base at New London, Conn., to investigate the stibine content of storage battery gases. U. S. National Institutes of Health, Bethesda, Md. (*Coordinate Navy Project X–166, Rept. no. 1*), 9 June 1943, 13 pp.

2615. Webster, S. H., E. J. Liljegren, and D. J. Zimmer. An interim report on the stibine study. U. S. National Institutes of Health, Bethesda, Md. (*Coordinate Navy Project X–166, Rept. no. 4*), 15 June 1944, 37 pp.

2616. Webster, S. H., E. J. Liljegren, and D. J. Zimmer. An interim report on the stibine study. U. S. National Institutes of Health, Bethesda, Md. (*Coordinate Navy Project X–166, Rept. no. 5*), 23 May 1945, 30 pp.

2617. Webster, S. H., E. J. Liljegren, D. J. Zimmer, and R. C. Dunn. The toxicology of stibine. National institute of arthritis and metabolic diseases, U. S. National Institutes of Health, Public Health Service, Bethesda, Md., 4 October 1951, 193 pp.

9. TOBACCO SMOKE

Smoking has become a virtually universal habit, and the use of tobacco has certain definite morale values. Conditions of submarine operation, however, impose certain definite restrictions upon smoking. The study of the physiological and pathological effects of tobacco constitutes an important field of investigation which cannot be discussed in detail here. From the large body of literature on this subject, only a few representative reports are discussed and considered. The major effects of tobacco are due to its nicotine content. However, tobacco smoke also contains a definite amount of carbon monoxide and it appears also that the resins present in tobacco smoke may exert a significant action, particularly when taken into the lungs over a prolonged period. The action of tobacco smoke may be adverse when added to unfavorable environmental conditions such as low oxygen and high carbon dioxide content of the air. Smoking may also be inadvisable under conditions of stress and intense bodily activity. Moreover, there are certain pathological conditions in which smoking is contraindicated. For a general consideration of tobacco, a chapter by Osol and colleagues (*2628*) 1947 may be consulted. Attention is drawn to the action of nicotine in producing peripheral vasoconstriction with a rise in blood pressure. There is also an inhibition of hunger contractions resulting in a diminution of appetite. Salivary and gastric secretion may be increased. There is also an increased output of epinephrine with an increase in the blood-sugar level. Extreme views on the biological hazards of tobacco smoking are expressed by Mills (*2626*) 1950 who cites the opinion that smoking predisposes to pulmonary tuberculosis. He also claims an abnormally high incidence of cigar and pipe smoking in male victims of malignant disease of the upper and lower respiratory passages. Postoperative pneumonia is stated to be more frequent among smokers than nonsmokers, and the author quotes the view that patients with peptic ulcer should abstain from smoking. He also states that smoking is a handicap to nursing mothers, and voices the opinion that smoking mothers are more likely to bear malformed infants than those who do not smoke. There is no confirmation in the literature for this view regarding malformation. Mills states that only tobacco smokers are afflicted with thromboangitis obliterans, and this is virtually true.

In a report on some effects on the circulation of smoking cigarettes with varying nicotine content, Mather, Patterson, and Levy (*2624*) 1949 have pointed out that the degree of reaction varies directly with the nicotine content of the smoke. There is a definite individual difference in the response,

and the variability in response in different persons is stated to depend to a greater extent upon individual susceptibility than upon the presence of cardiac disease. Acceleration of the heart is the most sensitive index of the nicotine effect, and a measure of individual differences in susceptibility is possible on a single reading. The authors suggest that an increase in the heart rate of 25 beats per minute after smoking one cigarette with inhalation may be regarded as evidence of hypersensitivity to the immediate effects of nicotine. The authors have found that smoking cigarettes with a nicotine content as low as 0.23 percent results in a significant heart-rate increase. In 1935, Lampson (*2623*) carried out a quantitative study of peripheral vasoconstriction induced by smoking. He determined peripheral blood flow in human subjects by recording changes in hand volume. Blood pressure and pulse were also recorded. Normal young men and patients from the peripheral circulatory clinic of the Massachusetts General Hospital, Boston, were the subjects. With one exception, smoking produced marked reduction of peripheral circulation in both the normal individuals and patients with thromboangitis obliterans. Smoking and inhaling cigarette smoke caused a sudden marked peripheral vasoconstriction, lasting about 60 minutes. When inhaling was avoided there was vasoconstriction lasting, however, only 15 minutes. So-called "denicotinized" cigarettes were found to produce less effect than ordinary cigarettes. Cigar and pipe smoking also induced vasoconstriction. Patients with thromboangitis obliterans responded in the same manner as normal subjects. The author recommended that smoking was contraindicated in patients with peripheral vascular disease.

Evans and Stewart (*2619*) 1943 also found that normal male subjects experienced a decrease in peripheral blood flow as a result of smoking, regardless of the type of cigarette smoked. After cessation of smoking, the peripheral blood flow continued to decrease in some cases, but began to return to normal levels in other cases. In all subjects a return toward normal had begun by the end of 30 minutes after cessation of smoking. Evans and Stewart found that the increase in blood pressure and pulse rate was essentially of the same magnitude and duration from smoking every type of cigarette. The average skin temperature decreased in all but five experiments. Herrell and Cusick (*2621*) 1938 emphasized the significance of the vasospastic response following inhalation of tobacco smoke among those who have a tendency towards hypertension, and stated that such a patient has everything to gain and nothing to lose by discontinuing the use of tobacco. These authors have demonstrated photographically the vasospactic changes in the retina. Mulinos and Shulman (*2627*) 1940 concluded that deep breathing alone can account for the greater part of the decreased blood flow rate, loss of hand volume, and drop of skin temperature resulting from the inhalation of cigarette smoke. The subjects who did not inhale cigarette smoke showed a greater vascular response of the hand from 10 deep breaths than from puffing the cigarette, and a lesser response than those who inhaled the cigarette smoke. Inhaling smoke from so-called denicotinized cigarettes resulted in as great a vasoconstriction as inhaling smoke from a standard-brand cigarette. Occasionally the vasoconstrictor effect from the "denicotinized" cigarettes was greater. These authors also draw attention to significant individual differences in susceptibility to cigarette smoke. For further reports on the effect of smoking on circulatory and respiratory phenomena, papers by Jourdan and Collet (*2622*) 1951 and Mecl and Sramek (*2625*) 1950 should be consulted.

The effect of smoking in diminishing hunger has been explained by Haggard and Greenberg (*2620*) 1934 as an action of nicotine on the adrenal glands with a production of hyperglycemia. These authors' study was carried out on human subjects and should be consulted. For an experimental study of the effect of nicotine on maze learning ability of albino rats, the reader is referred to a report by Essenberg (*2618*) 1948.

2618. Essenberg, J. M. The effect of nicotine on maze learning ability of albino rats. *Fed. Proc. Amer. Soc., exp. Biol.*, 1948, *7:* 31–32.

2619. Evans, W. F. and H. J. Stewart. The effect of smoking cigarettes on the peripheral blood flow. *Amer. Heart J.*, 1943, *26:* 78–89. [P]

2620. Haggard, H. W. and L. A. Greenberg. The effects of cigarette smoking upon the blood sugar. *Science,* 1934, *79:* 165–166.

2621. Herrell, W. E. and P. L. Cusick. Vascular and retinal abnormalities following inhalation of tobacco smoke: preliminary report. *Proc. Mayo Clin.*, 1938, *13:* 273–279. [CH]

2622. Jourdan, F. and A. Collet. Effects comparés de l'inhalation de fumée de tabac par les voies respiratoires supérieures et par les poumons chez le chien. *C. R. Soc. Biol., Paris,* 1950, *144:* 861–863. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1359.

2623. Lampson, R. S. A quantitative study of the vasoconstriction induced by smoking. *J. Amer. med. Ass.*, 1935, *104:* 1963–1966.

2624. Mather, J. A. L., M. C. Patterson, and R. L. Levy. Some effects on the circulation of smoking cigarettes with varying nicotine content. *Amer. Heart J.*, 1949, *37:* 612–619. [P]

2625. Mecl, A. and J. Sramek. Účinek nikotinu na pracovní výkon obéhu krevního a dýchání. [The effect of cigarette smoking on the circulation and respiration at work.] *Arch bohèm. méd.*, 1949, *51:* 377–410. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1443.

2626. Mills, C. A. Tobacco smoking: some hints of its biologic hazards. *Ohio St. med. J.*, 1950, *46:* 1165–1170.

2627. Mulinos, M. G. and I. Shulman. The effects of cigarette smoking and deep breathing on the peripheral vascular system. *Amer. J. med. Sci.*, 1940, *199:* 708–719. [P]

2628. Osol, A., G. E. Farrar, E. E. Leuallen, W. F. Verwey, H. W. Youngken, D. K. Detweiler, and H. C. Wood, Jr. Tobacco, pp. 1631–1633 in: *The dispensatory of the United States of America.* 24th edition, Philadelphia, J. B. Lippincott Co., 1947, 1928 pp.

10. ORGANIC SOLVENTS

(a) Benzene

Benzene is one of the best organic solvents known, and is widely used for the purpose of dissolving grease from small parts and for other extraction purposes. Therefore, benzene may be present on the submarine and does constitute a potential health hazard. The acute symptoms from inhaling a high concentration of benzene may begin with a sense of exhilaration followed by drowsiness, fatigue, dizziness, nausea, and headache. If exposure is prolonged or if higher concentrations are inhaled, there may be tonic-clonic spasms succeeded by paralysis and loss of consciousness. The respiration at first becomes rapid but soon slows, and there may be circulatory collapse. The victim of severe exposure may succumb quickly from respiratory paralysis. The chronic inhalation of even small amounts of benzene may be potentially dangerous. The classical picture of chronic benzene poisoning is a profound anemia, loss of clotting capacity with resultant hemorrhage and loss of white blood cells and substances concerned with the defense of the organism against infection. There may also be a regenerative response to the destructive effect of benzene, and a normal red and white blood cell count may indicate only a compensatory action which veils the chronic destruction. In workers suffering from chronic benzene poisoning, the harmful effects can occur in advance of detectable blood changes, and may even continue to develop after removal from exposure. In persons poisoned by benzene, the bone marrow may be normal, aplastic, or hyperplastic. The maximum allowable concentration of benzene in the atmosphere has been generally accepted at 100 p.p.m. However, Hardy and Elkins (*2630*) 1948 have stated that 75 p.p.m. of benzene is too high, and that the maximum permissible concentration should be reduced to 35 p.p.m. They recommended that workers exposed to benzene should have routine complete blood studies done and that there should be a routine preemployment medical evaluation including history of repeated infections, chronic blood loss, and ingestion of drugs known to depress bone-marrow activity. The hematological base line should be established by laboratory study and a follow up blood count should be done at intervals, depending upon the circumstances of benzene exposure. For further reports on benzene poisoning, papers by Foulger (*2629*) 1949 and Hutchings, Drescher, McGovern, and Coombs (*2631*) 1947 may be consulted.

2629. Foulger, J. H. Physiologic effects of industrial solvents. *J. Amer. med. Ass.*, 1949, *139:* 826–829.

2630. Hardy, H. L. and H. B. Elkins. Medical aspects of maximum allowable concentrations: benzene. *J. industr. Hyg.*, 1948, *30:* 196–200.

2631. Hutchings, M., S. Drescher, F. B. McGovern, and F. A. Coombs. Investigation of benzol and toluol poisoning in Royal Australian Air Force workshops. *Med. J. Aust.*, 1947, *2:* 681–692. [P]

(b) Carbon Tetrachloride

The use of carbon tetrachloride as a cleaning solvent for greasy equipment may incur severe poisoning effects following the use of this fluid in poorly ventilated working areas. Cases of nephrosis due to carbon tetrachloride inhalation are described in the literature cited below.

2632. Abbott, G. A. and M. J. Miller. Carbon tetrachloride poisoning. A report on 10 cases at the U. S. Marine Hospital, Seattle, Wash., since 1937. *J. industr. Hyg.*, 1949, *31:* abstract section: 102. *Publ. Hlth. Rep., Wash.*, 1948, *63:* 1619–1624. [CH].

2633. Amouroux, P. L'intoxication par les extincteurs d'incendie au gas ardexine. *Rev. Méd. nav.*, 1948, *3:* 133–147. [D]

2634. André, L. Intoxication par le tétrachlorure de carbone dans la marine. *Rev. Méd. nav.*, 1946, *1:* 213–234. [D] [CH]

2635. Elkins, H. B. Maximal allowable concentrations. I. Carbon tetrachloride. *J. industr. Hyg.*, 1942, *24:* 233–235. [CH]

2636. Farrier, R. M. and R. H. Smith. Carbon tetrachloride nephrosis. A frequently undiagnosed cause of death. *J. Amer. med. Ass.*, 1950, *143:* 964–967. *Abstr. World Med.*, 1950, *8:* 585.

2637. Glynn, L. E. and H. P. Himsworth. The intralobular circulation in acute liver injury by carbon tetrachloride. *Clin. Sci.*, 1948, *6:* 235–245. [P]

2638. Gray, I. Carbon tetrachloride poisoning. Report of seven cases with two deaths. *N. Y. St. J. Med.*, 1947, *47:* 2311–2315. [CH]

2639. King, B. G. High concentration-short time exposures and toxicity. *J. industr. Hyg.*, 1949, *31:* 365–375. [R]

2640. Laqueur, W. and F. Nashat. Dietary protein and carbon tetrachloride intoxication. Histological changes in the rat's liver in acute poisoning. *Arch. int. Pharmacodyn.*, 1948, *78:* 449–455. *Abstr. World Med.*, 1949, *6:* 148.

2641. Lehmann, K. B. and F. Flury. Carbon tetrachloride. pp. 145–154 in: *Toxicology and hygiene of industrial solvents.* Translated by E. King and H. F. Smyth, Jr. Baltimore, The Williams & Wilkins Co., 1943, 378 pp.

2642. McCord, C. P., J. H. Sterner, L. L. Kline, and P. E. Williams. The thymol-barbital test in experimental carbon tetrachloride poisoning. *Occup. Med.,* 1946, *1:* 160–167. [P]

2643. Moon, H. D. Pathology of acute carbon tetrachloride toxicity. *Amer. J. Pathol.,* 1949, *25:* 788–789. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 252.

2644. Moon, H. D. The pathology of fatal carbon tetrachloride poisoning with special reference to the histogenesis of the hepatic and renal lesions. *Amer. J. Pathol.,* 1950, *26:* 1041–1057. [CH]

2645. Mushett, C. W. Influence of crystalline vitamin B_{12} on carbon tetrachloride poisoning. *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 339.

2646. Reed, J. V. and A. K. Harcourt. Carbon tetrachloride CCl_4. pp. 31–34 in: *The essentials of occupational diseases.* Springfield, Charles C. Thomas, 1941, 225 pp.

2647. Sirota, J. H. Carbon tetrachloride poisoning in man. I. The mechanisms of renal failure and recovery. *J. Clin. Invest.,* 1949, *28:* 1412–1421. [R] [P]

2648. Stewart, A. and L. J. Witts. Chronic carbon tetrachloride intoxication. *Brit. J. industr. Med.,* 1944, *1:* 11–19. [CH]

2649. Sundareson, A. E. Protective action of nucleic acid on the liver in carbon tetrachloride poisoning. *J. Indiana med. Assn.,* 1948, *17:* 287–290. [P]

2650. Thompson, C. M. Pulmonary changes in carbon tetrachloride poisoning. *Amer. J. Roentgenol.,* 1946, *55:* 16–19.

2651. Wilson, R. H. Diagnosis and treatment of industrial solvent poisoning. *J. Amer. med. Assn.,* 1949, *139:* 906–909.

2652. Woods, W. W. The changes in the kidneys in carbon tetrachloride poisoning, and their resemblance to those in the "crush syndrome." *J. Path. Bact.,* 1946, *58*: 767–773. [M] [R] [CH]

11. OTHER NOXIOUS AGENTS

For references concerning other toxic gases and substances, the reader is referred to the following papers.

2653. Baetjer, A. M. Chronic exposures to air pollutants and acute infectious respiratory diseases. *Arch. ind. Hyg. occup. Med.,* 1950, *2:* 400–406.

2654. Baetjer, A. M. Atmospheric pollution. pp. 1010–1021 in: *Rosenau preventive medicine and hygiene.* Edited by Kenneth F. Maxcy. Seventh edition. Appleton-Century-Crofts, Inc., New York, 1951, 1462 pp.

2655. Cauer, H. Chemical climatology of the trace substances in the air of submarines. pp. B: II–1—B: II–108 in: *Monograph on submarine medicine, Folio II,* Germany, U. S. Zone. Office of naval advisor. 1948.

2656. Finland, M., M. Ritvo, C. S. Davidson, and S. M. Levenson. Roentgenologic findings in the lungs of victims of the Cocoanut Grove disaster. *Amer. J. Roentgenol.,* 1946, *55:* 1–15. [CH]

2657. Gray, M. G. Toxicity of ozone under simulated industrial conditions. *Fed. Proc. Amer. Soc. exp. Biol.,* 1949, *8:* 296.

2658. Lushbaugh, C. C., J. W. Green, Jr., and C. E. Redemann. Effects of prolonged inhalation of oil fogs on experimental animals. *Arch. industr. Hyg. occup. Med.,* 1950, *1:* 237–247. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1950, *3:* 1580.

2659. Osol, A., G. E. Farrar, E. E. Leuallen, W. F. Verwey, H. W. Youngken, D. K. Detweiler, and H. C. Wood, Jr. Acrolein. pp. 1306–1307 in: *The dispensatory of the United States of America.* 24th edition, Philadelphia, J. B. Lippincott Co., 1947, 1928 pp.

2660. Schaefer, K. E. Technical influences. II. Condensation droplets, ions and gamma-rays contained in the air of submarines. pp. B: I–38—B: I–50 in: *Monograph on submarine medicine,* Folio I, Germany, U. S. Zone. Office of naval advisor. 1948.

2661. Sendroy, J., J. D. O'Neal, and G. C. Pitts. Composition and effect of vapors emanating from insulated electrical equipment under conditions of simulated submarine operation. U. S. Navy. NMRI. *Project NM004 005.02.01,* 8 August 1950, 22 pp. [P]

2662. Shea, T. E., Jr., G. C. Pitts, and J. D. O'Neal. Effect of temperature and operation time upon the production of noxious gases from silicone insulated electrical equipment under conditions of simulated submarine operation. U. S. Navy. NMRI. *Project X–755, Rept. no. 1,* 9 December 1947, 6 pp. [P]

2663. Thorp, C. E. The toxicity of ozone. A report and bibliography. *Industr. med surg.,* 1950, *19:* 49–57.

2664. U. S. Army. Chemical Corps. Medical Division. Health hazards of propellant fuels and treatment therefor. *Project 4–16–17–01, Summary Rept.,* 30 June 1949, 35 pp. [P]

VII. MOTION SICKNESS

A. GENERAL STUDIES ON MOTION SICKNESS

Of the general references to motion sickness listed below, particular attention is called to articles by the following authors: Bard (*2667*) 1948; Chapanis, Garner, and Morgan (*2669*) 1949; Hemingway (*2673*) 1945; McEachern, Morton, and Lehman (*2674*) 1942; Schwabb (*2677*) 1940; Spiegel and Sokalchuk (*2678*) 1950; Tufts College (*2679*) 1949; and Tyler and Bard (*2680*) 1949.

Tyler and Bard's review (*2680*) sets forth the subject of motion sickness in detail. These authors point out that motion sickness became of utmost importance during World War II when vast numbers of men were being carried to combat zones or were flying. Animals as well as men are subject to motion sickness, and it is believed that almost any human being can be made ill if the stimuli are sufficiently strong. Dogs are especially susceptible and are similar to human beings in their susceptibility. Monkeys and cats are very resistant. Susceptibility appears to depend upon a rather specific constitutional capacity to respond to certain patterns of vestibular stimulation and can be modified by several extralabyrinthine influences. About 95 percent of susceptible persons are capable of adaptation to motion. Adaptation to one type of move-

ment does not necessarily adapt the individual to motion produced by a different device or vessel. It is estimated that 3 to 5 percent of the population are extremely susceptible to motion sickness and cannot be adapted. Experimental methods of producing motion sickness use devices which reproduce movements of ships, elevators, and swings. Apparatus which rotates and tilts the head may also be used. Composite motion is more effective than any one type. It appears that the most significant structure concerned in the production of motion sickness is the labyrinth. Bilateral labyrinthectomy will render susceptible dogs immune to motion sickness. Human deaf-mutes, lacking in labyrinthine reactions, are generally not susceptible to motion sickness. The labyrinthine sense organs essentially involved in motion sickness are the cristae of the semicircular canals and the utricular maculae. Addition of small angular accelerations to a motion which has only linear changes in velocity augments its nauseating properties. Motion sickness can be produced by either angular or linear accelerations, the semicircular canals being involved in the former and the utricles being stimulated in the latter. Any head position in which the vertical canals assume a nearly horizontal position is the least conducive to the production of swing sickness. It has been shown that extirpation of the cerebellum or portions of the cerebellum prevents motion sickness in animals. The central nerve pathway apparently leads from the labyrinth to the vestibular nuclei in the medulla, and thence to cerebellar, thalamic, and spinal centers. Vagal centers in the medulla are also essentially involved. The extent of cortical involvement is uncertain, and experimental studies show that decortication does not affect susceptibility to motion sickness. Psychological factors appear to have very little to do with the cause of motion sickness. No entirely satisfactory tests for preselecting motion-sickness-resistant candidates for submarine, flight, or other military training have yet been devised. It has been recommended that actual motion sickness in the early phases of operational training is the most practical selective procedure.

2665. Antunez, N. Mal de mar y su tratamiento. pp. 192–196 in: *Higiene naval y nociones de anatomia y fisiologia.* Moret, La Coruna, 1950, 321 pp.

2666. Babkin, B. P., and S. Dworkin. Experimental studies of motion sickness. Canada NRC. Proceedings of conference on motion sickness, *Project 736,* 28 August 1942, 9 pp.

2667. Bard, P. Motion sickness. pp. 278–295 in: Part III. Aviation Medicine in: *Advances in Military Medicine, Vol. I.* Edited by E. C. Andrus, D. W. Bronk, G. A. Carden, Jr., C. S. Keefer, J. S. Lockwood, J. T. Wearn, and M. C. Winternitz. Boston, Little, Brown and Co., 1948, 472 pp. [R]

2668. Blackham, R. J. Sea-sickness. *Brit. med. J.,* 1939, *2:* 163–167. [R]

2669. Chapanis, A., W. R. Garner, and C. T. Morgan. The working environment. The effects of motion. pp. 408–414 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

2670. Cipriani, A. and D. McEachern. Montreal motion sickness machine. Canada NRC. Proceedings of conference on motion sickness. *Project C615,* 28 August 1942, 5 pp.

2671. Dragotti, G. Rivista sintetica; il mal di movimento. *Policlinico.* 1948, *55:* 1329–1336. [D]

2672 Green, D. M. Air sickness in bomber crews. *J. Aviat. Med.,* 1943, *14:* 366–372.

2673. Hemingway, A. Survey of research on the problem of air sickness in the Army Air Forces. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 381, Rept. no. 1,* 20 April 1945, 45 pp. [R]

2674. McEachern, D., G. Morton, and P. Lehman. Sea sickness and other forms of motion sickness. I. A general review of the literature. *War Med., Chicago,* 1942, *2:* 410–428. [R]

2675. Monaco, L. Per i passeggeri che coffrono di mal d'aria. *Riv. Med. aero.,* 1947, *10:* 370–372. [D]

2676. Rubin, H. J. Air sickness in a primary air force training detachment. *J. Aviat. Med.,* 1942, *13:* 272–276.

2677. Schwab, R. S. Motion sickness. pp. 664 (54–20)–664 (54–30) in: *Oxford medicine,* Vol. IV, Part III. Edited by H. A. Christian. New York, Oxford University Press, 1940. [R]

2678. Spiegel, E. A. and A. Sokalchuk. Motion sickness. pp. 572–580 in: *Medical physics, Vol. II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

2679. Tufts College. Motion sickness. 6 pp. in: *Handbook of human engineering data for design engineers.* Tufts College, Institute for applied experimental psychology. *SDC Human Engineering Project 20–G–1, Project Designation NR–783–001, Technical Report 199–1–1,* 1 December 1949, 410 pp.

2680. Tyler, D. B. and P. Bard. Motion sickness. *Physiol. Rev.,* 1949, *29:* 311–369. [R]

2681. U. S. NRC–CAM. Bibliography of air sickness and sea sickness. Bibliography of labyrinthine studies in relation to motion sickness. List of reports of British flying personnel research committee (F. P. R. C.) and of the National Research Council, Canada, in relation to motion sickness up to September 1942. *C. A. M. Rept. no. 82,* November 1942, 44 pp. [B]

2682. U. S. Navy, ONR. Psychophysiology Branch. Report of conference on motion sickness. 9 September 1950, 15 pp.

B. SIGNS AND SYMPTOMS OF MOTION SICKNESS (PHYSIOLOGICAL AND PATHOLOGICAL CHANGES)

For general studies of the symptomatology of motion-sickness, papers by the following should be consulted: Brett (*2684*) 1942, Howlett (*2688*) 1942, and Palmisano (*2691*) 1951. Cold sweating in motion sickness has been investigated by Hemingway (*2685*) 1944 by an electrical device which measures the onset of sweating. A calcium chloride water absorption device was also used to measure the rate of sweating. In Hemingway's study, subjects were men between the ages of 20 and 30 who

had passed the Army physical examination. The men were subjected to periodic motion involving changing linear and centrifugal accelerations varying between 1.0 and 2.0 g. It was found that sweating occurred as a result of motion, and at the same time the mouth temperature fell. According to Hemingway, there appears to be no physiological purpose in cold sweating, and the motion sickness mechanism is probably a part of a primitive defense reaction. In a further study by Hemingway (*2686*) 1945, motion sickness was produced in normal young men by means of a 20-minute swing test. Blood pressure, pulse rate, body and skin temperature, and the rate of sweating were measured. Motion sickness was not associated with any significant change in systolic pressure, diastolic pressure, or pulse rate. Cold sweating was present during motion sickness with a drop in skin and mouth temperature, and this was seen in environments with air temperatures near freezing. Hyperventilation frequently occurred with tingling sensations in the feet and hands, and occasionally carpopedal spasm. In a few instances the latter was so severe that the hands were "frozen" to the supports and the fingers had to be pried loose. X-ray examination after a barium meal showed loss of gastric tone and delayed emptying of the stomach associated with motion sickness. In a further report, Hemingway (*2687*) 1945 reported that of a group of 489 normal young adults who were exposed to the swing, sickness occurred in 29 percent of those tested. There was a slight tendency for elevation of blood pressure immediately following vomiting, but otherwise (as just stated) there were no significant changes in systolic pressure, diastolic pressure, or pulse rate associated with motion sickness.

Sokalchuk (*2694*) 1947 reported blood-pressure readings in seasick crew members of a destroyer subjected to a combination of rolling, pitching, yawing, and up and down motion. An average of 6 percent of the men became seasick. In 37 men, systolic and diastolic blood pressures were repeatedly measured in port and during seasickness. Rise as well as fall of the systolic pressure appeared in five cases. Fall in the systolic pressure of 1 to 10 mm. of Hg was more frequent (15 cases) than a corresponding rise (2 cases). Fifteen men showed an average fall of 11 to 27 mm. of Hg, and 13 men showed a maximal fall of more than 15 mm. of Hg. The reaction of the diastolic pressure was somewhat similar.

Ventilation rates and respiratory patterns during exposure to the swing test for motion sickness have been studied by Rushmer (*2693*) 1943. Ventilation rates were recorded on 35 subjects. In 15 subjects, respiratory movements and period of the swing were simultaneously recorded to determine how frequently they tended to breathe in rhythm with the motion of swing. Ventilation rates were found almost invariably to be elevated during the swing test. The increase tended to be greater in persons suffering from symptoms of motion sickness than in those subjects not so affected by the swing test. There was a poor correlation in this group of subjects between increase in ventilation rate and subjective complaint of symptoms. With one exception, every subject tended to synchronize respiratory rhythm with the motion of the swing. Overventilation was not considered of importance in the etiology of swing sickness. Several subjects exhibiting the greatest increases in ventilation rates during the swing test admitted they were apprehensive and excited during the test.

Regarding the effect of swinging on motility of the stomach, Babkin and Bornstein (*2683*) 1943 have carried out experimental studies on dogs. A combination of a horizontal and vertical acceleration with a minimum of rotatory movement produced motion sickness in dogs susceptible to this form of disturbance. Swinging of dogs susceptible to motion sickness immediately inhibited all the movements of the fasting stomach, as evidenced by cessation of hunger contractions and a fall of gastric tone. Continuation of swinging induced vomiting within 5 to 15 minutes. The aftereffect of swinging in animals susceptible to motion sickness was, in the minority of cases, a gradual recovery of gastric tone and return of hunger contractions. More often, there appeared within 15 to 120 minutes special rhythmic contractions of the stomach which developed gradually with lowered tone. This latter form of gastric hypermotility was not affected by atropine and could not be induced by prostigmine. In a dog less susceptible to motion sickness, swinging likewise arrested the hunger contractions, but vomiting did not occur until after about 2 hours of continuous swinging. The special rhythmic contractions of the stomach appeared during swinging, but they were relatively weak and irregular. Bilateral labyrinthectomy abolished all symptoms of motion sickness in the susceptible dogs. It was concluded, therefore, that the chief cause of the diverse phenomena observed in the stomach during horizontal and vertical acceleration is excessive stimulation of the vestibular apparatus.

Repeated vomiting associated with motion sickness may have serious consequences. Pumphrey, Kuh, Johnson, and Day (*2692*) 1946 reported the case of a 25-year-old crewman aboard an attack transport who was seasick for 3 days. He vomited repeatedly and hyperventilated. His arms and

fingers became stiff, and he fell unconscious with carpopedal spasm. He was given 20 cc. of 10 percent calcium gluconate and rebreathed into a paper bag. There was relaxation of the spasm within 10 minutes. A slight chill with vomiting supervened. One thousand cu. cm. of 5 percent glucose in saline were given.

For vestibular symptoms, papers by Lewy (*2689*) 1947 and Palmisano (*2690*) 1951 may be consulted.

2683. Babkin, B. P. and M. B. Bornstein. The effect of swinging on the motility of the stomach in dogs. Canada NRC. Proceedings of second meeting of associated committee on naval medical research. *Project C4030,* 7 October 1943, 12 pp.

2684. Brett, J. R. Symptomatology of swing sickness. Canada NRC. Proceedings of conference on motion sickness. *Appendix "R" 5f,* 28 August 1942, 1 p.

2685. Hemingway, A. Cold sweating in motion sickness. *Amer. J. Physiol.,* 1944, *141:* 172–175.

2686. Hemingway, A. Physiological changes during motion sickness. *Fed. Proc. Amer. Soc. exp. Biol.,* 1945, *4:* 33.

2687. Hemingway, A. Cardiovascular changes in motion sickness. *J. Aviat. Med.,* 1945, *16:* 417–421. [P]

2688. Howlett, F. A. L. Symptomatology of air sickness. Canada NRC. Proceedings of conference on motion sickness. *Appendix "R" 5d,* 28 August 1942, 3 pp. [P]

2689. Lewy, A. The symptomatology of vertigo. *Ann. Otol., etc., St. Louis,* 1947, *56:* 534–540.

2690. Palmisano, C. Ossevazioni sulla fisiopatologia neuro-vegetativa, vestibolare e oculare nella naupatia, di soggetti imbarcati su navi di superficie. *Ann. Med. nav. trop.,* 1951, *56:* 164–176.

2691. Palmisano, C. Studio delle caratteristiche oculari e dei riflessi oculari neurovegetativi in condizioni di mare calmo e ricerche sulle loro variazioni fisio-patologiche nella naupatia, in soggetti imbarcati su navi di superficie *Ann. Med. nav. trop.,* 1951, *56:* 687–710. [P]

2692. Pumphrey, R. E., J. R. Kuh, M. A. Johnson, and A. L. Day. Unusual conditions aggravated by sea sickness. *Nav. med. Bull., Wash.,* 1946, *46:* 742–743. [CH]

2693. Rushmer, R. F. Overventilation in subjects during the swing test. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 133, Rept. no. 1,* 1 May 1943, 6 pp. [P]

2694. Sokalchuk, A. Blood pressure in seasickness. *Fed. Proc. Amer. Soc. exp. Biol.,* 1947, *6:* 207. [P]

C. SUSCEPTIBILITY TO MOTION SICKNESS

Birren (*2699*) 1949 has pointed out that it is improbable that a totally motion-sickness-resistant group could ever be screened because of the large population of persons who may be made motion sick. Susceptibility to motion sickness may be regarded as a general factor for all situations involving acceleration. With available means of detecting susceptibility to motion sickness, including questionnaires and surveys, a significant reduction could be made in the number of unadaptable or very susceptible persons being assigned to critical tasks in the services. Although there are striking individual differences in susceptibility to motion sickness, the basis for these differences is not entirely apparent. Few individual traits, either physiological or psychological, have been found to be related to susceptibility. Personality factors do not contribute in an important degree to variations in susceptibility. Motion sickness is not a psychological affliction, although there appear to be persons in whom unusual emotional stress may favor the onset of symptoms.

Hemingway (*2710*) 1946 has discussed a number of methods for evaluating susceptibility to motion sickness. The Barany chair test has been abandoned. History of motion sickness may be of value, but should not by itself be used as a reason for rejecting a candidate. The swing test is a simple method for producing motion sickness and is superior to the motion-sickness history in its correlation with incidence of airsickness. Hemingway believes that the swing-test results should by themselves not be considered disqualifying. He considers the record of airsickness in flight training the best means of evaluating motion-sickness susceptibility. He has recommended that the motion-sickness history and the swing-test results be considered in preflight evaluation for flying fitness, and that the airsickness record be kept for the first 10 flights. If the trainee is airsick once after the fifth flight, the case should be reviewed for possible elimination. If the trainee is sick twice after the fifth flight, he should be eliminated. In general, it would seem that these recommendations are valid.

A number of reports have appeared in the literature on the value of the motion-sickness history in predicting airsickness or other forms of motion sickness under operational conditions. For such studies, papers by the following should be consulted: Alexander, Cotzin, Hill, Ricciuti, and Wendt (*2695*) 1945; Birren (*2698*) 1947; Birren and Fisher (*2700*) 1947; Birren, Fisher, and Stormont (*2701*) 1944; Howlett and Brett (*2712*) 1942; and Mathewson (*2721*) 1942. Beginning with the early years of World War II, histories of previous motion sickness were derived from men subjected to the swing test as well as those interviewed at flying schools in the various services both in the United States and abroad (*2712*). Mathewson (*2721*) 1942 pointed out that it was impossible by the history method to ascertain accurately the prevalence of susceptibility to motion sickness. He found that the incidence of positive histories increased as the inquiries became more searching. From data assembled from a closely supervised group of 308 men, it would appear that some correlation exists between a previous history of motion sickness and

airsickness occurring during flight training. The positive correlation depends to a large extent on the care with which the history was obtained. Birren, Fisher, and Stormont (*2701*) 1944 administered a motion-sickness questionnaire to 277 male naval personnel whose susceptibility to motion sickness was known from the person's own judgment of his susceptibility, from susceptibility ratings of men by officers at sea, and from judgment of boards of medical survey. From an item analysis of the questionnaire it appeared that susceptibility to motion sickness is a rather specific factor. No evidence was found of a correlation between general psychosomatic complaints and susceptibility to motion sickness. Alexander, Cotzin, Hill, Ricciuti, and Wendt (*2695*) 1945 reported a series of five experiments, using a total of 477 naval officer candidates, in which the incidence of motion sickness resulting from a 20-minute exposure of blindfolded subjects on a vertical accelerator was analyzed for its relationship to previous history of motion sickness as determined by a questionnaire. The overall results showed a reliable and moderately high relation between motion-sickness history and experimentally produced sickness. The results were interpreted by the authors as indicating that machine sickness has factors in common with other forms of motion sickness. It was also suggested that a questionnaire might yield a useful prediction of motion sickness in military situations and might be used as an elimination or selection device.

As a result of an experimental study with a revised motion-sickness questionnaire, Birren (*2698*) 1947 believed it of sufficient validity and reliability to screen out those who would be severely affected by motion sickness. There was a tendency for men to rate themselves more susceptible than did their associates. No relation was found between questions of general somatic and psychosomatic import and susceptibility to seasickness. There was no indication that fear of naval duty was related to susceptibility to seasickness. There seems little evidence to justify a purely psychogenic interpretation of motion sickness. In 48 men incapacitated for sea duty because of extreme susceptibility to motion sickness, the most distinctive group was sensitive to all forms of motion sickness. The group was also characterized by excessive body sway, proneness to nausea and vomiting from the action of centrally acting emetic drugs, and ease with which symptoms were produced on a rolling platform. No severe psychological defects were revealed which could account for susceptibility. Results of a questionnaire given to 1,560 male naval personnel suggest that motion sickness is relatively common. Distress, nausea, and vomiting are produced by a wide variety of situations involving periodic motion. Birren and Fisher (*2700*) 1947 studied the validity of the questionnaire method by comparing the questionnaire scores of 150 officers and men with sea experience on a destroyer as reported by officers who were in a position to know the relative susceptibility to seasickness of each man. About 10 percent of the 150 men were indicated as highly susceptible. A person's questionnaire score correlated more highly with his own estimate of susceptibility than with another individual's estimate of his susceptibility. The 10 percent of the destroyer-escort crew having the highest questionnaire scores included about half of those who were rated highly susceptible to seasickness. Elimination of this 10 percent would therefore have reduced the number of susceptibles from 10 in 100 to about 5 in 100. Greater predictive efficiency of the questionnaire was indicated when self-judgments, rather than judgments by associates, were used as the criterion. It was concluded by the authors that the questionnaire seems to have sufficient validity and reliability for screening out persons very susceptible to seasickness. Brown, Brett, and Howlett (*2703*) 1943 concluded that use can be made of a well-taken history of susceptibility to motion sickness in indicating those men who may experience airsickness in flight training.

The swing test for the production of motion sickness has been used both in experimental animals and in man. Induced motion-sickness techniques have provided not only a method whereby the mechanisms of motion sickness may be studied but also have permitted differentiation of the persistently motion-sick group from the non-motion-sick group with fair accuracy. For studies of the relation of swing-test results to actual incidence of motion sickness in military operations, papers by the following authors should be consulted: Fields (*2705*) 1942; Hemingway (*2707*) 1943; Hemingway (*2708*) 1943; Hemingway (*2709*) 1946; Howlett (*2711*) 1942; Howlett and Brett (*2713*) 1942; Jasper, Battista, Bornstein, and Noble (*2716*) 1943; McDonough (*2719*) 1943; Morton (*2722*) 1942; Morton, Cipriani, and McEachern (*2723*) 1942; and Noble (*2726*) 1948.

Attempts to establish a significant relationship between psychological defects and susceptibility to motion sickness have not yielded reliable positive findings (*2730*). Wendt (*2729*) 1949 believes that no absolute distinction can be made between psychological and physiological factors in motion sickness. Factors such as the character of the motion, the position of the head, and the physiological state

as affected by drugs, are considered the major determiners of motion-sickness rates. Army and Navy subjects did not become motion sick unless the combination of physiological and physical factors was appropriate. The author concluded that, although psychological factors are demonstrably operative, physical and physiological factors outweigh them in practical importance. Wendt has stressed the need of a better understanding of the kinds of motion sickness and a better understanding of the physiology of motion sickness so that prophylactic drugs may be more adequately studied.

A number of factors have been investigated in relation to motion-sickness susceptibility. Head position and character of motion have been investigated by Morton and McEachern (*2724*) 1942. In these authors' studies, vertical up and down motion with the head fixed in the erect position provided the situations most likely to cause motion sickness. Birren, Stormont, and Pfeiffer (*2702*) 1945 have studied reactions to neostigmine and apomorphine as an indication of susceptibility to seasickness. Neostigmine was administered intramuscularly to 14 control subjects and to 14 enlisted personnel surveyed to shore duty because of chronic seasickness. Vomiting did not occur in either group. The symptomatology following neostigmine did not aid in distinguishing between the seasick susceptibles and the normals. Apomorphine was administered subcutaneously to 18 controls and 22 chronic seasickness personnel. Nausea and vomiting occurred in 7 of the 22 seasick susceptible subjects and in 3 of the 18 control subjects. Reactions elicited after administration of apomorphine thus allowed a very rough differentiation between susceptibility and nonsusceptibility to seasickness.

Birren (*2697*) 1945 initiated observations on the basis for susceptibility to seasickness on 48 men who were so susceptible to seasickness that they were unable to work effectively at sea. These men were given a series of tests, three of them involving equilibrium. The susceptible men were not different from the normal seamen in their ability to balance themselves in the railwalking test which requires the subject to walk a 10-foot 1-inch wide rail. Postrotational nystagmus was slightly, but not significantly, longer in the susceptible men for both the horizontal and vertical positions in the Barany chair. The falling reaction to the vertical position appeared exaggerated in several of the susceptible men. The Barany chair test as a whole did not bring out any striking differences between the normal and susceptible men. A difference did appear between the susceptible and normal men in the amount of body sway.

It seems from studies of Goehring (*2706*) 1942 and Benedict and Schwab (*2696*) 1945 that men suffering from seasickness or who are susceptible to seasickness show characteristic abnormalities of the stomach and duodenum (loss of gastric motility and spasm of the pyloric sphincter) as examined by X-ray. Kirkner (*2718*) 1949 attempted to design a test for the prediction of airsickness on the hypothesis that skin resistance changes characteristically during spatial displacement. Various stimulations were used including subcutaneous injection of apomorphine, caloric irrigation, rotation, and swabbing the throat with a light cotton swab. The most violent vomiting reaction was obtained with apomorphine. The data failed to show any consistent relationship between sweating and relative decrease in palmar resistance. According to the data, a relative decrease in palmar resistance does not appear to be a reliable measure of the rate of sweating or of nausea. It was concluded that relative palmar resistance change is not a satisfactory measure for nausea induced by labyrinthine stimulation.

According to Jasper and Morton (*2717*) 1942, there is no significant correlation between instability in electroencephalographic records and past history of motion sickness. Thorner (*2728*) 1943 concluded that the electroencephalogram cannot be used effectively as a means of preselecting navigation cadets who will be most susceptible to airsickness, although the electroencephalograms of airsickness-susceptible groups differ markedly from those of a corresponding group of healthy adults in the general population. Morton, McNally, and Stuart (*2725*) 1942 carried out caloric tests on 31 subjects and concluded that there is no definite correlation between the reaction to minimum caloric stimulation and susceptibility to motion sickness, unless the nystagmus, nausea, and vomiting are unusually severe.

For further studies on susceptibility to motion sickness, papers by the following should be consulted: Eyer (*2704*) 1943, Howlett and Brett (*2714*) 1942, Howlett and Brown (*2715*) 1942, MacPhee and Pennington (*2720*) 1946, and Schwab (*2727*) 1942.

2695. Alexander, S. J., M. Cotzin, C. J. Hill, Jr., E. A. Ricciuti, and G. R. Wendt. Wesleyan University studies of motion sickness: VI. Prediction of sickness on a vertical accelerator by means of a motion sickness history questionnaire. *J. Psychol.*, 1945, *20:* 25–30. [P]

2696. Benedict, E. B. and R. S. Schwab. Gastroscopic studies in naval personnel with chronic seasickness. *New Engl. J. Med.*, 1945, *233:* 237. [CH]

2697. Birren, J. E. Equilibrium and susceptibility to seasickness. *Fed. Proc. Amer. Soc. exp. Biol.*, 1945, *4:* 7.

2698. Birren, J. E. Psychophysiological studies of motion sickness. Abstract: *Northwestern University, Summaries of doctoral dissertations,* 1947, *15:* 254–257.

2699. Birren, J. E. Motion sickness: its psychophysiological aspects. pp. 375–414 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

2700. Birren, J. E., and M. B. Fisher. Susceptibility to seasickness: a questionnaire approach. *J. appl. Psychol.,* 1947, *31:* 288–297. [P]

2701. Birren, J. E., M. B. Fisher, and R. T. Stormont. An evaluation of a motion sickness questionnaire in predicting susceptibility to seasickness. U. S. Navy. NMRI. *Project X–278, Rept. no. 2,* 15 August 1944, 8 pp. [P]

2702. Birren, J. E., R. T. Stormont, and C. C. Pfeiffer. Reactions to neostigmine and apomorphine as indication of susceptibility to seasickness. U. S. Navy. NMRI. *Project X–278, Rept. no. 4,* 26 February 1945, 9 pp. [P]

2703. Brown, B. R., J. R. Brett, and J. G. Howlett. Swing sickness and a history of motion sickness in relation to airsickness. Canada NRC. Proceedings of a conference on motion sickness. *Project C2504,* 18 May 1943, 8 pp.

2704. Eyer, A. W. The incidence of airsickness among aviation cadets in patrol aircraft. U. S. Navy. NATC., Pensacola, Fla. School of aviation medicine. *Project no. X–72 (Av–F10–1),* 29 January 1943, 10 pp. [P]

2705. Fields, W. S. Induced motion sickness in naval ratings. Canada NRC. Proceedings of conference on motion sickness. *Project C738,* 28 August 1942, 5 pp. [P]

2706. Goehring, H. D. Gastrointestinal tract in seasickness. U. S. Navy. Naval Hospital, Chelsea, Mass. *Project no. X–375,* 26 December 1942, 3 pp. [P]

2707. Hemingway, A. Incidence of swing sickness in eight categories of army personnel. U. S. AAF. Randolph Field, Texas. School of aviation medicine. *Project 170, Rept. no. 1,* 30 July 1943, 3 pp. [P]

2708. Hemingway, A. Motion sickness history and results of the swing test of one hundred and seven (107) airsick eliminees from flight training. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 170, Rept. no. 2,* 7 September 1943, 6 pp. [P]

2709. Hemingway, A. The relationship of airsickness to other types of motion sickness. *J. Aviat. Med.,* 1946, *17:* 80–85, 95. [P]

2710. Hemingway, A. Selection of men for aeronautical training based on susceptibility to motion sickness. *J. Aviat. Med.,* 1946, *17:* 153–163. [P]

2711. Howlett, F. A. L. Swing test followup. Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5i,* 28 August 1942, 1 p.

2712. Howlett, F. A. L. and J. R. Brett. History of motion sickness and its relation to airsickness. Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5c (2),* 28 August 1942, 1 p.

2713. Howlett, F. A. L. and J. R. Brett. Airsickness investigation (A. S. 5). Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5g,* 28 August 1942, 6 pp.

2714. Howlett, F. A. L. and J. R. Brett. Blood pressure and motion sickness. Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5j,* 28 August 1942, 2 pp. [P]

2715. Howlett, J. G. and B. R. Brown. Incidence of airsickness at training schools. Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5b,* 28 August 1942, 2 pp. [P]

2716. Jasper, H. H., A. Battista, M. Bornstein, and R. H. Noble. Reliability of the swing test of motion sickness. Canada NRC. Proceedings of second meeting of associated committee on naval medical research. *Project C4038,* 7 October 1943, 3 pp.

2717. Jasper, H. H. and G. Morton. Electroencephalography in relation to motion sickness in volunteers. Canada NRC. Proceedings of conference on motion sickness. *Project C745,* 28 August 1942, 2 pp.

2718. Kirkner, F. J. Psychophysiological studies of motion sickness and airsickness. *J. comp. physiol. Psychol.,* 1949, *42:* 273–285. [P]

2719. McDonough, F. E. Airsickness in navigation training. U. S. NRC–CAM. *C. A. M. rept. no. 181,* 5 July 1943, 18 pp.

2720. MacPhee, H. M. and L. A. Pennington. The identification of cases of chronic motion sickness during military screening examinations. *J. soc. Psychol.,* 1946, *23:* 61–64.

2721. Mathewson, F. A. L. History of motion sickness and relationship to incidence of airsickness. Canada NRC. Proceedings of conference on motion sickness. *Appendix R, 5c,* 28 August 1942, 3 pp. [P]

2722. Morton, G. Susceptibility of animals to induced motion sickness. Canada NRC. Proceedings of conference on motion sickness. *Project C746,* 28 August 1942, 1 p. [P]

2723. Morton, G., A. Cipriani, and D. McEachern. Susceptibility to motion sickness in volunteers. Canada NRC. Proceedings of conference on motion sickness. *Project C742,* 28 August 1942, 5 pp. [P]

2724. Morton, G. and D. McEachern. Experimental studies on a susceptible individual. Canada NRC. Proceedings of conference on motion sickness. *Project C750,* 28 August 1942, 2 pp. [P]

2725. Morton, G., W. J. McNally, and E. A. Stuart. Caloric vestibular tests in relation to susceptibility to motion sickness. Canada NRC. Proceedings of conference on motion sickness. *Project C743,* 28 August 1942, 1 p. [P]

2726. Noble, R. L. Adaptation to experimental motion sickness in dogs. *Amer. J. Physiol.,* 1948, *154:* 443–450. [P]

2727. Schwab, R. S. Chronic seasickness. Neurological, psychiatric, and naval aspects. *Nav. med. Bull., Wash.,* 1942, *40:* 923–936.

2728. Thorner, M. W. Cortical activity in airsick personnel. U. S. AAF. Randolph Field, Tex. School of aviation medicine, *Project 169, Rept. no. 1,* 24 July 1943, 6 pp. [P]

2729. Wendt, G. R. Of what importance are psychological factors in motion sickness? *J. industr. Hyg.,* 1949, *31:* abstract section: 69. *J. Aviat. Med.,* 1948, *19:* 24–32. [R]

2730. Zwerling, I. Psychological factors in susceptibility to motion sickness. *J. Psychol.,* 1947, *23:* 219–239.

D. MECHANISMS OF MOTION SICKNESS

For general studies on the mechanisms of motion sickness, papers by the following may be consulted: Byrne (*2742*) 1912, Cojazzi (*2744*) 1950, Harbert and Schiff (*2747*) 1950, Hatcher (*2748*) 1924, Morales (*2768*) 1949, and Sjoberg (*2773*) 1931. The volume by Byrne is a large, definitive work on the physiology of the semicircular canals and their relation to seasickness. Cojazzi's paper (*2744*) is an excellent critical review of present views on the

pathogenesis of seasickness and contains a long reference list. Sjoberg (*2773*) has prepared an article giving approximately 160 references on the general subject of motion sickness and the labyrinthine mechanism. Hatcher's long review (*2748*) gives a historical survey of the literature covering the mechanisms of vomiting itself. Harbert and Schiff (*2747*) have pointed out that motion sickness is not the result of stimulation of a single organ, but is the result of a break in accommodation by the spinal, medullary, and cerebellar centers from continual, unusual stimuli arising in several organs. In order of importance, the sensory stimuli are probably vestibular, proprioceptive, visual, and others. An important factor in this breakdown is a discrepancy in the sensations from various sources. Sensations from the labyrinth and so forth are not unpleasant by themselves. It is the abnormal reflexes produced by these sensations that are unpleasant. When the cerebellar, medullary, and spinal centers are repeatedly subjected to unusual stimuli, particularly when the stimuli are incompatible, a point is finally reached when they cause more than normal reflex responses. Morales' report (*2768*) discusses physical factors in the etiology of motion sickness and is concerned with the characteristics of the motion patterns as well as responses of the receptor systems.

Noble (*2770*) 1950 made extensive observations on the motion factors causing vomiting in dogs. He found horizontal motion to be most effective. The vertical component has some effect and the angular component probably none. No one component of motion was as effective as composite motion. The rate of horizontal motion was an important factor, resulting in an increased effect. The effectiveness of vertical movement in producing motion sickness could be increased by increasing the distance traversed. Increasing the rate was ineffective. Swings with six different radii and swinging through three different angles were reported. The optimum radius appeared to be about 14 feet, longer or shorter radii causing a diminution of susceptibility. Reducing the angle of swinging lowered the incidence of vomiting, except where a very short radius was used. In this case an increased response occurred, probably related to the increase in rate of swinging.

Wendt and his associates have carried out detailed studies to discover the physical conditions of motion sickness. Using a wave machine similar to an elevator, Alexander, Cotzin, Hill, Ricciuti, and Wendt (*2731*) 1945 exposed subjects to waves having a period of constant velocity during the up-and-down motions. It was found that a wave with a 1.1-second period of constant velocity produced the most sickness; it was concluded that the time interval between accelerations is a factor in production of motion sickness. Alexander, Cotzin, Klee, and Wendt (*2733*) 1947 used waves with constant acceleration of 0.2 g., the frequency being controlled by control of duration of application of upward and downward acceleration. By this means, wave frequencies of 13, 16, 22, and 32 cycles per minute were obtained, having amplitudes of 9 feet, 5 feet 4 inches, 2 feet 6 inches, and 1 foot 1 inch. Other significant variables were counterbalanced or controlled. Results on 120 subjects showed motion sickness varied with the energy per wave. The largest wave produced the most sickness, the smallest wave the least. Sickness rates of 37, 37, 10, and 7 percent were obtained in that order, proceeding from the large, slow wave to the small, fast wave. In general, it was found that some waves are as much as 20 times more nauseating than others per unit of energy. Motion-sickness-producing capacity depends upon at least four factors: (1) wave duration, (2) acceleration level, (3) distribution of acceleration, and (4) energy per wave. Fraser and Manning (*2746*) 1950 have examined the effects of variation in swing radius and arc upon the incidence of swing sickness. The incidence of swing sickness increased from 4 to 58 percent when the frequency was decreased from 22 per minute on a 6-foot swing to 15 per minute on a 16-foot swing. The incidence was reduced from 50 to 22 percent by reducing the oscillation angle from 90° to 50°, or by a *g* change from 0.9 to 0.25. Increasing the angle from 90° to 130° did not increase the incidence of swing sickness. The authors suggested that the tangential component of force on the swing was necessary for the production of motion sickness.

Body and head position affect susceptibility to motion sickness. Manning and Stewart (*2763*) 1942 and (*2764*) 1949 concluded from a series of 1005 swing experiments carried out on 825 men swung in 14 various body positions, that the maximal incidence of swing sickness occurs in the sitting position with the subject completely inclosed in a cabinlike arrangement. The minimal incidence occurred in the supine position with the eyes open. Apprehension, time of day, and meals did not appear to be factors affecting the occurrence of swing sickness. These experiments, according to the authors, support the view that motion sickness is primarily a labyrinthine disturbance which tends to be suppressed or compensated by visual orientation. Stewart and Manning (*2776*) 1943 stated that the sitting position with the head tilted back 90° from the horizontal is the least susceptible position on the

four-pole swing. Howlett, Wardill, and Brett (*2753*) 1943 carried out swing tests on 50 unselected air-crew trainees who were swung through an angle of 80° in the supine position with the head resting on the middle of the occiput and the reference plane perpendicular to the swing base. These trainees were also swung in the supine position through an angle of 62° with the head rotated backwards so that the reference plane formed an angle of 13° with the base of the swing. The incidence of swing sickness was low when the subjects were swung through an angle of 80° in the supine position with the head resting on the middle of the occiput and with the reference plane perpendicular to the swing base. According to Johnson, Stubbs, Kelk, and Franks (*2754*) 1951, individual susceptibility to motion sickness produced by a simple harmonic swing shows a significant correlation with the degree of concomitant head movement. Swing sickness, according to the authors, can be almost totally overcome by preventing this head movement.

Regarding the sensory and central nervous mechanisms involved in motion sickness, a number of studies have been reported which are contributory. For such studies, papers by the following should be consulted: Barany (*2734*) 1910 and (*2735*) 1912; Bard (*2736*) 1945 and (*2737*) 1946; Bard, Woolsey, Snider, Mountcastle, and Bromiley (*2738*) 1947; Borison and Wang (*2740*) 1949; Howlett and Brett (*2752*) 1943; McNally (*2758*) 1944 and (*2759*) 1947; McNally and Stuart (*2760*) 1942; McNally, Stuart, and Morton (*2761*) 1942; Meda (*2766*) 1947; Morales (*2767*) 1946; Okawachi (*2771*) 1951; Palmisano (*2772*) 1951; Spiegel (*2774*) 1946; Spiegel, Oppenheimer, Henny, and Wycis (*2775*) 1944; Trotter (*2777*) 1946; Wang and Borison (*2778*) 1950; and Wendt (*2779*) 1951. The paper by Wendt (*2779*) is particularly useful as an excellent review of the history and development of research on vestibular functions.

The reports by Bard and colleagues (*2736, 2737* and *2738*) are of especial interest as casting fresh light upon the central nervous mechanisms. The role of the cerebral cortex was evaluated and tested (*2736*) and it was found that temporal, occipital, and parietal areas are not essentially involved in the motion-sickness mechanism. Bilateral temporal lobectomy, removal of both frontal poles, or ablation of all the neocortex except one or both frontal poles did not significantly alter susceptibility to motion sickness. The effect of complete decortication was not determined (*2738*). Decerebration by removing a wedge of tissue rostral to a plane passing from the anterior colliculi to a level just behind the mammillary bodies did not alter the emetic response to swing tests between 26 and 53 days following the operation. After uncomplicated removal of the entire cerebellum, a highly susceptible dog failed to vomit or show any premonitory symptoms in 15 tests carried out during a survival period of 17 months. Removal of the nodulus and uvula rendered very susceptible dogs immune, but did not affect the emetic response to apomorphine (*2737*).

A number of experimental investigations have been carried out to study physiological and chemical changes associated with motion sickness. For the most part, these studies have not yielded significant correlations that would permit the use of a physiological or chemical change in prediction of motion-sickness susceptibility. Cipriani and Morton (*2743*) 1942 found no constant or significant changes in heart rate, blood pressure, or respiratory rate as a result of motion. According to Best, Sellers, and Stephenson (*2739*) 1942, motion sickness does not cause a significant change in the acid-base balance in dogs. The level of ionized calcium does not seem to be connected in any way with the susceptibility of a dog to motion sickness. The potassium ion showed a slight decrease in dogs subjected to motion. High potassium or high sodium diet had no apparent effect on the susceptibility of dogs to motion sickness. There seemed to be a slight increase in plasma protein in motion-sick dogs, especially those that salivated profusely. There appeared to be little evidence to support chemical changes in the blood as important causes of motion sickness. According to Fields, Meakins, and McEachern (*2745*) 1942, there was no change in blood sugar, calcium, phosphorus, sodium, or potassium before and after motion in human subjects. Meakins, Morton, and McEachern (*2765*) 1942 found no changes in the carbon dioxide content, oxygen content, oxygen capacity, or oxygen saturation in pre- and post-motion specimens of arterial dog blood. These same findings were reported in 1942 by McEachern and Lehmann (*2757*). Morton, Cipriani, and McEachern (*2769*) 1947 reported that determinations of the sugar, phosphorus, and various bases in the blood in human subjects showed a moderate increase in sugar and a reduction of phosphorus as a result of motion. These changes occurred whether or not the subject became sick. They were attributed possibly to the liberation of epinephrine, due to motion or apprehension. Studies of gases in the arterial blood of animals revealed no significant changes as a result of motion. Cholinesterase determinations were carried out before and after swinging in human subjects who became motion sick in experiments carried out by Manning (*2762*). No significant

differences in cholinesterase activity before and after swing sickness in both airsick-susceptible and nonairsick individuals were found. For other studies on cholinesterase activity and its possible relation to motion sickness, papers by Himwick, Essig, Hampton, Bales, and Freedman (*2751*) 1949, and Laborit and Morand (*2755*) 1946 may be consulted.

For other reports on the mechanisms of motion sickness, papers by the following should be consulted: Alexander, Cotzin, Hill, Ricciuti, and Wendt (*2732*) 1945; Bortolotti (*2741*) 1940; Hemingway (*2749*) 1943 and (*2750*) 1946; and Landahl (*2756*) 1950.

2731. Alexander, S. J., M. Cotzin, C. J. Hill, Jr., E. A. Ricciuti, and G. R. Wendt. Wesleyan University studies of motion sickness: I. The effects of variation of time intervals between accelerations upon sickness rates. *J. Psychol.*, 1945, *19:* 49–62. [P]

2732. Alexander, S. J., M. Cotzin, C. J. Hill, Jr., E. A. Ricciuti, and G. R. Wendt. Wesleyan University studies of motion sickness: V. Incidence of sickness at various hours of the day. *J. Psychol.*, 1945, *20:* 19–24. [P]

2733. Alexander, S. J., M. Cotzin, J. B. Klee, and G. R. Wendt. Studies of motion sickness: XVI. The effects upon sickness rates of waves of various frequencies but identical acceleration. *J. exp. Psychol.*, 1947, *37:* 440–448. [P]

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2735. Bárány, R. Die Seekrankheit. pp. 864–873 in: *Handbuch Der Neurologie. Dritter Band Spezielle Neurologie II.* Edited by M. Lewandowsky. Berlin, Verlag Von Julius Springer. 1912, 1165 pp. [D]

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2737. Bard, P. Motion sickness. *Johns Hopk. Hosp. Bull.*, 1946, *79:* 359–360. [P]

2738. Bard, P., C. N. Woolsey, R. S. Snider, V. B. Mountcastle, and R. B. Bromiley. Delimitation of central nervous mechanisms involved in motion sickness. *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 72. [P]

2739. Best, C. H., E. A. Sellers, and N. R. Stephenson. Seasickness—animal experiments. Canada NRC. Proceedings of conference on motion sickness. *Project C735,* 28 August 1942, 21 pp. [P]

2740. Borison, H. L., and S. C. Wang. Localization of the central nervous mechanism of emesis. *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 13.

2741. Bortolotti, R. Il VII nel punto di passaggio dalla seconda alla sua terza porzione. *Rass. ital. Otorinolaring.*, 1940, *14:* 11–32.

2742. Byrne, J. *On the physiology of the semicircular canals and their relation to seasickness.* New York, J. T. Dougherty, 1912, 569 pp.

2743. Cipriani, A., and G. Morton. Studies of blood pressure, electrocardiograms, and respiratory tracings in volunteers. Canada NRC. Proceedings of conference on motion sickness. *Project C744,* 28 August 1942, 3 pp. [P]

2744. Cojazzi, L. Attuali canoscenze sulla patogenesi del mal di mare. *Clin. otorinolaring.*, 1950, *2:* 357–383.

2745. Fields, W. S., J. C. Meakins, and D. McEachern. Blood chemistry studies in motion sickness. Canada NRC. Proceedings of conference on motion sickness. *Project C740,* 28 August 1942, 2 pp. [P]

2746. Fraser, A. M. and G. W. Manning. Effect of variation in swing radius and arc on incidence of swing sickness. *J. appl. Physiol.*, 1950, *2:* 580–584.

2747. Harbert, F. and M. Schiff. Motion sickness. *Armed Forces med. J.*, 1950, *1:* 979–984. [D]

2748. Hatcher, R. A. The mechanism of vomiting. *Physiol. Rev.*, 1924, *4:* 479–504. [R]

2749. Hemingway, A. The effect of environmental temperature on motion sickness. U. S. AAF. Randolph Field, Tex. School of aviation medicine. *Project 170, Rept. no. 3,* 2 November 1943, 4 pp. [P]

2750. Hemingway, A. Environmental temperature and swing sickness. *J. Aviat. Med.*, 1946, *17:* 86–88; 99. [P]

2751. Himwich, H. E., C. F. Essig, J. L. Hampson, P. D. Bales, and A. M. Freedman. Cholinergic nature of the vestibular receptor mechanism; forced circling movements (motion picture). *Fed. Proc. Amer. Soc. exp. Biol.*, 1949, *8:* 75.

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2755. Laboria, H. and P. Morand. L'activité cholinestérasique et son rôle probable dans le mal de mer. *Rev. Méd. nav.*, 1946, *1:* 23–24.

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2758. McNally, W. J. Recommendation for further investigation to be carried on in solving the problem of motion sickness. Canada NRC. Proceedings of third meeting of associate committee on naval medical research. *Project C4063,* 15 May 1944, 1 p.

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2760. McNally, W. J. and E. A. Stuart. Physiology of the labyrinth reviewed in relation to seasickness and other forms of motion sickness. *War Med., Chicago,* 1942, *2:* 683–771. [R]

2761. McNally, W. J., E. A. Stuart, and G. Morton. Effect of labyrinthectomy on motion sickness in animals. Canada NRC. Proceedings of conference on motion sickness. *Project C748,* 28 August 1942, 1 pp. [P]

2762. Manning, G. W. Choline esterase activity in relation to airsickness. Canada NRC. Proceedings of conference on motion sickness. *Project C2513,* 1 p. (summary.) [P]

2763. Manning, G. W. and W. G. Stewart. The effect of position on the incidence of swing sickness. Canada

NRC. Proceedings of conference on motion sickness. *Project C2511,* 12 December 1942, 2 pp. [P]

2764. Manning, G. W. and W. G. Stewart. Effect of body position on incidence of motion sickness. *J. appl. Physiol.,* 1949, *1:* 619–627. [P]

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2767. Morales, M. F. Asynchrony of labyrinthine receptors as a physical factor in motion sickness. *Bull. math. Biophys.,* 1946, *8:* 147–157. [M]

2768. Morales, M. F. Motion sickness: physical considerations regarding its etiology. pp. 399–414 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

2769. Morton, G., A. Cipriani, and D. McEachern. Mechanism of motion sickness. *Arch. Neurol Psychiat., Chicago,* 1947, *57:* 58–70.

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2774. Spiegel, E. A. Effect of labyrinthine reflexes on the vegetative nervous system. *Arch. Otolaryng., Chicago,* 1946, *44:* 61–72. [R]

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2777. Trotter, W. R. Sea sickness. *Practitioner,* 1946, *157:* 45–49. [R]

2778. Wang, S. C. and H. L. Borison. The vomiting center; a critical experimental analysis. *Arch. Neurol. Psychiat., Chicago,* 1950, *63:* 928–941. *XVIII Intern. physiol. Congr.,* 1950, 503–504. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 1129.

2779. Wendt, G. R. Vestibular functions, pp. 1191–1223 in: *Stevens—Handbook of experimental psychology.* New York, John Wiley & Sons, Inc., 1951, xi. 1436 pp. [R]

E. EFFECT OF MOTION SICKNESS ON PERFORMANCE

Practical experience under combat conditions reveals that motion sickness may seriously impair performance. This performance deficit is, however, difficult to demonstrate significantly under laboratory test conditions. Effects of exposure to experimental motion upon performance of laboratory motor performance tests have been studied by Alexander, Cotzin, Hill, Ricciuti, and Wendt (*2780*) 1945. Certain performance tests were administered to human subjects before and after exposure to motion on the vertical accelerator. The data were analyzed to determine whether those who became motion sick showed deficits in performance. Of four tests used, only one, the Mashburn Complex Coordinator, showed a statistically reliable harmful effect of motion sickness, the obtained deficit being about 4 percent. These results were interpreted by the authors as indicating that brief exposure to motion for 20 minutes or until vomiting occurred probably had no important effects upon laboratory motor performance tests.

2780. Alexander, S. J., M. Cotzin, C. J. Hill, Jr., E. A. Ricciuti, and G. R. Wendt. Wesleyan University studies of motion sickness. VII. The effects of sickness upon performance. *J. Psychol.,* 1945, *20:* 31–39.

F. PREVENTION AND TREATMENT OF MOTION SICKNESS

Search for effective motion-sickness-preventive drugs and effective combinations of these drugs has gone on for many years. Investigation of motion-sickness preventives was accelerated during World War II; and, as the reference list given below indicates, these studies are continuing unabated. A number of drugs, such as hyoscine, dramamine, other antihistaminics, and the barbiturates, are recognized as effective. Some studies seem to indicate that certain combinations of these drugs may be particularly effective, and other synthetic substances have also been under test. While these substances may reduce the incidence of motion sickness, they may produce undesirable side effects, such as somnolence, which may render personnel unfit for various types of military duty while under the influence of the drugs. For example, it is not desirable that aviators be in the actual control of aircraft while under the influence of motion-sickness-preventive drugs. Passengers in aircraft, surface vessels, and submarines may safely take motion-sickness drugs, provided that the effects of these substances will have worn off by the time such personnel are required to carry out essential military duties. For papers on the general sub-

ject of prevention and treatment of motion sickness, the following references may be consulted: *2782, 2788, 2789, 2790, 2793, 2794, 2795, 2803, 2804, 2810,* and *2812.*

The use of hyoscine has been investigated as indicated in the following references: *2784, 2785, 2792, 2796, 2797, 2800, 2802, 2806, 2807, 2808, 2809, 2813, 2815, 2819, 2825, 2832, 2833, 2838, 2839, 2840, 2841, 2842, 2843, 2848, 2849, 2854, 2855, 2856, 2857, 2858, 2859, 2863, 2864, 2874, 2876, 2882, 2883, 2885, 2886, 2890, 2891, 2893,* and *2894.*

For studies on dramamine, the following references are given: *2805, 2818, 2821, 2822, 2823, 2826, 2836, 2837, 2844, 2845, 2847, 2865, 2866, 2868, 2871, 2872, 2873, 2887, 2888, 2889, 2896, 2898, 2900,* and *2901.*

Studies on other antihistaminic drugs are given in the following references: *2798, 2799, 2801, 2820, 2831, 2834, 2835, 2860, 2867, 2873, 2884, 2895,* and *2899.*

The barbituric acid derivatives have been used singly and in combination with other substances. Studies on these compounds are reported in the following references: *2814, 2829, 2850, 2852, 2853, 2861, 2879, 2880, 2881,* and *2892.*

The following substances have also been used in the prevention of motion sickness: pyridoxine (*2878*), sodium bicarbonate and other inorganic compounds (*2787, 2817* and *2828,* and bromides (*2786*).

For other studies on motion-sickness prevention, the following references may be consulted: *2781, 2791, 2811, 2816, 2824, 2827, 2830, 2846, 2851, 2862, 2869, 2870, 2875, 2877,* and *2897.*

2781. Albrecht, F. K. A therapeutic evaluation of benzedrine sulfate in the treatment of seasickness: results in 100 cases. *Med. Clin. N. Amer.*, 1943, Philadelphia number: 1652–1658.

2782. Alvarez, J. S. A. Estado actual de la fisiopatologia y tratamiento del mal de mar. *Medicina, Madr.*, 1949, *17:* 223–235.

2783. Ambrus, J. L. and C. M. Ambrus. Motion sickness and antihistamines, *Lancet,* 1950, *258:* 326. *Excerpta Medica, Section II.* (*Physiology, Biochemistry, and Pharmacology*), 1950, *3:* 969.

2784. Amouroux, P. Traitement du mal du mer par les seasickness tablets. *Rev. Méd. nav.*, 1947, *2:* 167–168. [D]

2785. Armstrong, H. G. Treatment of air sickness. *Postgrad. Med.*, 1950, *8:* 55–56. [D]

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2788. Beckman, Harry. Effectiveness of newer drugs in seasickness. pp. 392–394 in: *The 1950 Year Book of Drug Therapy.* Chicago. The Year Book Publishers, Inc., 1951, 566 pp.

2789. Beckman, Harry. Effectiveness of various drugs in prevention of airsickness. pp. 394 in: *The 1950 Year Book of Drug Therapy.* Chicago. The Year Book Publishers, Inc., 1951, 566 pp. [P]

2790. Birren, J. E., R. T. Stormont, and M. B. Fisher. Side effects of three motion sickness preventives. U. S. Navy. NMRI. *Project X–278, Rept. no. 1.* 26 June 1944, 7 pp. [P]

2791. Birren, J. E., R. T. Stormont, and C. C. Pfeiffer. An evaluation of the potentiality of bulbocapnine as a motion sickness preventive. U. S. Navy. NMRI. *Project X–278, Rept. no. 3.* 16 August 1944, 5 pp. [D]

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2797. Chinn, H. I. and F. W. Oberst. Effectiveness of various drugs in prevention of airsickness. 1. Effects of chemical components of dramamine. USAF, Randolph Field, Tex. School of aviation medicine. *Project 21–32–014* (*formerly project 21–02–169*), *Rept. no. 1,* August 1950, 5 pp. [P]

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2800. Chinn, H. I. and B. A. Strickland, Jr. Effectiveness of various drugs in prevention of airsickness. II. Comparison of hyoscine with benadryl-hyoscine mixture during navigation training flights. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–32–014, Rept. no. 2* (*formerly project 21–02–169*), December 1950, 3 pp. [P]

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VIII. SUBMARINE ESCAPE PROBLEMS

A. BREATH HOLDING

All submariners, divers, and underwater swimmers in the U. S. Navy are trained to use the submarine escape apparatus (referred to as the "lung") at the escape training tank, Submarine Base, New London, Conn., or the Submarine Base, Pearl Harbor, T. H. Free escape, that is to say, escape without the use of any apparatus, is also practiced by the instructors at the escape training tanks and certain of the more proficient trainees. With regard to free escape, correct breath control is absolutely essential. The air in the lungs must be exhaled rather slowly to begin with, and then with steadily increasing volume so as to avoid dangerously high positive pressure in the lungs. If exhalation is impaired, there may be an excess pressure sufficient to tear the lung tissue. Too rapid exhalation slows the ascent rate and may destroy positive buoyancy. However, it is considered safer to err on the side of too rapid exhalation, since lost buoyancy can relatively easily be compensated for by swimming up a few strokes. The references on breath holding which follow have been included and are discussed here because of the manifest importance of breath control in escape and because from the literature on breath holding are to be derived data of importance needed for the design and operation of escape apparatus and underwater swimming gear.

The breath-holding breakpoint at various increased pressures has been reported by Alvis (*2904*) 1951. His investigation was undertaken to determine what factors force a person to inspire when he voluntarily holds his breath. It was hypothesized that carbon dioxide accumulation might be the critical factor rather than blood pH or oxygen depletion when the partial pressure of oxygen was above some undetermined level. It was further hypothesized that the blood pH would not vary significantly under increased pressure or during a series of breath holds conducted within an elapsed time of 1 to 2 hours. Alveolar carbon dioxide tension was found to be a more consistent value

at the breath-holding breakpoint than alveolar oxygen tension or duration of breath holding. This was found to be true for various increased ambient pressures. Subjects were found to be able to hold their breath after breathing air for longer periods and to higher alveolar carbon dioxide tension levels as the ambient pressure was increased. Oxygen was presumed to play no important role in limiting breath holding beyond 33 feet depth. Rahn, Otis, and Fenn (*2909*) 1947 and Otis, Rahn, and Fenn (*2910*) 1948 found that at high oxygen tensions the breath-holding time was long, whereas at low oxygen tensions (corresponding to an altitude of 18,000 feet) breath-holding time was short.

In a respiratory and circulatory study during breath holding, Muxworthy (*2908*) 1950 found in trained subjects that a linear relationship does not exist between lung volume and the maximum time of apnea. At the breakpoint of breath holding, the carbon dioxide tension was higher with the greater lung volumes while the oxygen saturation remained approximately the same. The smaller lung volumes resulted in lower carbon dioxide tension while there was little change in oxygen saturation of the blood as compared to breath holding with lung volumes within the range of normal tidal volume. The carbon dioxide tension is higher and the oxygen tension lower during exercise, both with normal respiration and at the end of maximum breath holding, as estimated from alveolar air samples. The heart rate decreased as the blood pressure increased during breath holding, and did not begin to increase until the pressure decrease during the recovery period reached approximately the same level that stimulated the rate to decrease. Rate of blood flow, pulse volume, and total finger volume all indicate that vasoconstriction occurs during breath holding and lasts about 8 to 10 seconds beyond the breakpoint. Stroud (*2911*) 1950 found that establishment of acidosis by ingestion of 15 grams of ammonium chloride a day for 3 days resulted in shorter breath-holding time than normal. The resting alveolar carbon dioxide tension was lowered and the oxygen tension increased, and at the breakpoint the carbon dioxide tension was lower in all cases.

For further reports on breath holding, papers by the following may be consulted: Akira (*2902, 2903*) 1950, André and Boxus (*2905*) 1947, Fenn and DuBois (*2906*) 1950, and Montoye (*2907*) 1951.

2902. Akira, N. Studies on the breath holding. (6) On the comparison of the breath holding with the rebreathing. *Nihon Seiri. Z.*, 1950, *12:* (Japanese text pagination), 121–127. (English text pagination), 127. (In Japanese with English summary.)

2903. Akira, N. Studies on the breath holding. (7) Influence of the inhalation of pressed air on the human body. *Nihon Seiri. Z.*, 1950, *12:* (Japanese text pagination), 128–131. (English text pagination), 131. (In Japanese with English summary.)

2904. Alvis, H. J. Breath-holding breakpoint at various increased pressures. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 014.01, Rept. no. 1,* 10 August 1951, 10 pp.

2905. André M. J. and V. Boxus. Le temps d'apnée voluntaire du sujet sain dans diverses conditions experimentales. *Rev. belge Path.*, 1947, *18:* 42–77. [P]

2906. Fenn, W. O. and A. B. DuBois. Carbon dioxide in the alveolar air, muscles and bones. *XVIII Intern. physiol. Congr.*, 1950: 199–200.

2907. Montoye, H. J. An analysis of breath-holding tests. *Res. Quart Amer. Phys. Educ. Ass.*, 1950, *21:* 322–330. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 881.

2908. Muxworthy, J. F., Jr. *A respiratory and circulatory study during breath holding.* Thesis, (Physiol.) University of Rochester. Rochester, New York. 1950, 64 pp. [P]

2909. Rahn, H., A. B. Otis, and W. O. Fenn. Alveolar gas changes during breath holding. *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 183. [P]

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B. ESCAPE PROCEDURES

For reports on training in escape procedures and a commentary on actual escapes in a submarine disaster, a paper by Willmon, Duff, and Shilling (*2917*) 1947 should be consulted. An ONI report (*2916*) 1951 also contains a general discussion of submarine escape. The former paper describes the submarine training tank and the submarine escape apparatus. The authors consider that training with the submarine escape apparatus not only provides a sense of security but also a prognostic test for identifying personnel not adapted to submarine service. The history is given of an accident off Formosa in 1944 when the U. S. S. *Tang* was sunk by its own torpedo. The boat sank quickly by the stern and remained for 15 minutes at least at a very acute angle, the stern resting on the bottom and the bow sticking out of water. The upper conning tower hatch was open as the boat sank. Those in the control room managed to shut the lower conning tower hatch, but it was strained by the explosion and leaked. The confusion at this stage with men and gear falling around due to the acute angle was great. All but two of those in the conning tower were probably drowned almost at once. One of these two found himself breathing in an airpocket. He struggled out of this and reached

a larger pocket at the forward end of the conning tower. Very shortly thereafter this officer ducked out from his airpocket and made a successful free ascent through the conning tower hatch without breathing apparatus or lifebelt. The officer had been instructed in the technique of exhaling during free ascent at the submarine school. He described his ascent as follows: "I began to swim up, using both hands as hard as I could. The whole idea was to get up. I wanted air and lots of it. I had no sensation of being under pressure, but thought about letting the air out, and knew as I came up that I would have to force the air out so I heaved it out all at once and then just as I thought I would have to swallow some salt water I burst out on the surface and began swimming." He was none the worse, had no pains in his chest, and swam around for about 8 hours before he was picked up. The second man alive in the conning tower was dazed and frightened. He was to have held on to the officer's trouser leg as he ducked out, but appears to have let go and was probably drowned without attempting to escape. Meanwhile, many men were alive (probably about 45 in the control room and compartments forward, and in the engineroom and after battery room). Approximately 15 to 30 minutes after the accident, an enlisted man in the control room opened a tank vent by hand and the submarine sank to the bottom and leveled off without any very serious angle. The depth was now 180 feet. The men made their way forward until 45 of them were collected in the forward torpedo room. One of them had his face smashed in when the door into the forward torpedo room was opened. The emergency lights were working. Not long after this an officer and some men tried to pass through the door aft, but as they cracked the door dense smoke and fumes poured in through the door. This smoke was serious for some time. Men complained of irritation of throat and lungs and eyes and seemed actually to choke to death in it. One survivor stated that this smoke did more to kill the men who did not get out than any other thing. Within 20 minutes or so, however, these conditions improved. There seems little doubt that there was a bad battery fire in the forward battery room which continued right up to the end as the lower part of the bulkhead at the after end of the torpedo room got hotter and hotter until the paint began to peel. There had previously been another fire forward when the forward plane rigging and tilting motor burned out completely. There was probably a continuous buildup of pressure from the flooded portion aft as the escape proceeded. Some survivors were said to have noticed the heightened pressure, but there was no definite evidence of it. The first attempt to escape from the forward torpedo room was made about 4 hours after the accident, and the last about 6 to 7 hours after the accident. In all, it seems that five attempts to escape were made. In the first attempt, four men entered the escape trunk taking a rubber boat with them. There was a difference of opinion among them as to procedures. There was also difficulty in getting the line out. One man did not wait for the line and went out alone. This man had already been injured about the head in the first crash and is reported to have used his escape apparatus and taken two pistols and a bayonet with him. He was not seen again, and whether he reached the surface is not known. Some 40 minutes later, as there was no signal from the trunk, those in the compartment drained it down. The three remaining in the trunk must therefore have been under pressure equal to 180 feet of water for 40 minutes. The failure of the three men to escape after 40 minutes in the trunk must have discouraged those in the compartment, especially as one of them stated that he did not care to attempt the escape again. Summarizing the escapes from the forward torpedo room, it appears that probably 13 tried to escape, and 8 or 9 reached the surface and 5 survived. Of those who died on the surface, one was probably already injured, one had been exposed to a pressure 180 feet of water for a long time twice, and all had been subjected to rising pressure and smoke inside the submarine for several hours.

Commenting upon this disaster, Willmon, Duff, and Shilling recommended that provisions must be made for vocal communication between the escape trunks and adjacent compartments. Personnel in the compartment did not know what trouble those in the trunk were having. It was also recommended that an oxygen supply be provided for the escape trunk. Emergency lights were controlled from below instead of being turned on from the trunk. This should be corrected. It was considered important that personnel know that in the absence of oxygen, compressed air or even one's own breath can be used to fill the submarine escape apparatus. Also personnel should know that free escape can be made in event the "lung" comes loose. All officers should be indoctrinated in escape procedures, and all personnel should be given detailed instruction on how to operate the escape trunks. The authors felt that more leadership training was needed to handle such stressful situations.

Reports of survivors from the German submarine, *U–1195,* sunk in April 1945 in the English channel off the Nab, provide valuable data of significance

in planning safer escape procedures and more realistic escape training. This boat was submerged at approximately 75 feet when she was holed by a depth charge forward. She rested on the bottom in 96 feet of water. All of the crew were alive, approximately 50 in all. These split into two parties. One lot of 33 went into the afterpart, the remaining 17 went into the control room. Out of the conning tower and control room 6 reached the surface and survived, 3 were without Draeger gear and 3 with it. It is of interest that these 3 with Draeger gear were submerged completely for what must have been several minutes before they could come out of the conning tower. Of the 50 crew members alive in the submarine after she sank, 14 actually came to the surface and lived. Of these, 7 came up with no Draeger gear, 1 came up using the Draeger only as a lifebelt with the mouthpiece cock shut, and the remaining 6 had Draeger gear in operation. Six had survived from the control room and conning tower, 6 from the twill trunk hatch, and 2 from the afterhatch with no twill trunk at all. An escape via the twill trunk may be described in some detail: This escapee was an officer. As his oxygen bottle was not working, he blew up his Draeger bag with his mouth while his head was in the air at the top of the compartment. The compartment had been flooded so that the twill trunk hatch could be opened. The officer took a deep breath and tried to get out, but was caught by his gear fouling the twill trunk. He repeated the procedure a second time and again got caught. The third time he went right under by holding on to the deck and got safely through the trunk. For the ascent he had his Draeger blown up as a lifebelt, the mouthpiece in his mouth but the mouthpiece cock shut. He stated afterwards that he put the mouthpiece into his mouth as the mouthpiece cock was leaking and he did not want the air to exhaust from his Draeger bag. He swallowed a little water during his struggle to get under and through the trunk. He considers that he must have been a minute struggling under the water before he got clear. After getting out, and on his way up, he let air escape out of his mouth as he had been taught. His minute of struggling in the trunk plus the air he had deliberately let escape finally made him want to breathe in before he reached the surface. Although he wanted to breathe in very badly he managed to keep his mouth firmly shut. Some water came in through his nose which finally stopped him trying to breathe in. He distinctly felt the expanding pressure in his lungs on his way up. He was in the water about 10 to 15 minutes before he was picked up on the surface. He stated that his eyes and the lower part of his chest hurt after the rescue. The pains in his chest made him feel that he could not get in enough air, but these pains subsided after about 20 minutes. His nose was permanently running for about 3 hours. He had no other pain and no visual disturbances, although his eyes continued to hurt him for a long while during cold weather. A survivor who made a free escape from the conning tower described in detail how he and the others were breathing very rapidly in a tiny airpocket immediately prior to opening the conning-tower hatch. He also stated he was unable to take a deep breath before leaving as there was so little air left and that this little amount contained much carbon dioxide. He stated that in this high concentration of carbon dioxide he found it very hard to hold his breath. Although he had been panting hard and found it difficult to breathe before the hatch was opened, as soon as he started ascending he no longer wanted to breathe in. As he ascended, he let air escape out of his mouth as he had been taught to do. He stated, "I just opened my mouth and away it went." He let out air all the way up. At first after leaving the boat he felt he was ascending too slowly. He therefore let more air into his life-jacket (presumably from a CO_2 cartridge). He then went up faster and at no time did he attempt to check his ascent. He felt no ill effects after reaching the surface. He stated quite clearly that he had no desire to inhale on the way up. On the contrary, he had too much air and wanted to get rid of it.

For descriptions of British escape procedures, papers by Davis (*2912*) 1951; Donald, Davidson, and Shelford (*2913*) 1948; and Taylor (*2915*) 1947 should be consulted. In evaluating self-contained escape apparatus, Davis (*2912*) stated that they should fulfill the following requirements: (1) they should be compact and light; (2) they should be instantly and easily put on; (3) they should have adequate air-regenerating devices to insure the wearer an air supply; (4) they should render him immune against poisonous gases; (5) they should be so designed as to allow the escapee free passage through hatchways; (6) they should permit him to breathe freely under water, no matter of what pressure; (7) they should be capable of retarding the velocity of ascent; (8) on the surface, they should provide buoyancy with the head up; and (9) they should not impede swimming progress. Escape training and procedures used in the Royal Navy are described. Two methods of escape are now used: (1) the collapsible trunk attached to an escape hatch, in which the whole compartment of the submarine is flooded (this is called the twill trunk); and (2) an escape chamber in which the escapees enter, 1 or 2 at a time

and which is flooded to enable them to emerge by an escape hatch. British escape procedures are further described by Donald, Davidson, and Shelford (*2913*). Considerable attention has been given to the procedure of free, unaided escape both by the U. S. Navy and the Royal Navy. A British report by Taylor (*2915*) 1947 describes uneventful free escapes made by goats from 220 feet and 300 feet. These results suggested to the author that for man such ascents are feasible. Reference may be made to a Russian report by Klimenko, Pavlovskii, and Maksimenko (*2914*) 1948. This report is to be found in the Soviet manual for divers of the navy, primarily a training manual. Means of escape are described and examples of escape are given. A submarine rescue chamber similar to the U. S. Navy chamber is explained. An escape training chamber resembling the training chamber at New London is diagramed and discussed.

2912. Davis, Robert H. Escape from sunken submarines. pp. 257–289 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., 1951, 670 pp. [D]

2913. Donald, K. W., W. M. Davidson, and W. O. Shelford. Submarine escape breathing air. *J. Hyg., Camb.*, 1948, *46:* 176–183. [P]

2914. Klimenko, N. A., K. A. Pavlovskii, and V. P. Maksimenko. Escape of personnel from the damaged submarine. pp. 136–169 in: *Manual for divers of the navy.* Moskow, Military Printing office, 1948, 172 pp. (Russian text.)

2915. Taylor, H. J. Simulated unaided ascents of goats in water from depths of (A) 220 feet, (B) 300 feet. Gt. Brit. MRC–RNPRC, UPS. *R. N. P. 47/348, U. P. S. 79,* January 1947, 2 pp. [P]

2916. U. S. Navy, ONI. Norway-Submarine personnel, training in escape procedures. *O. N. I. serial 62–U–51,* 12 June 1951, 2 pp.

2917. Willmon, T. L., I. F. Duff, and C. W. Shilling. Submarine escape ("lung") training pays off. pp. 199–214 in: *History of submarine medicine in World War II.* Edited by Shilling, C. W., and J. W. Kohl. U. S. Navy Submarine Base, New London, Conn. Medical research laboratory, 25 May 1947, 328 pp.

C. ESCAPE ACCIDENTS FROM SUBMARINES OR ESCAPE TRAINING TANKS

Excerpts from accounts of escape attempts from disabled submarines given in the previous section (p. 251) provide examples of the hazards involved. The operation of escape training tanks has continued over the years with a remarkable safety record. The following escape training fatal accident was reported by Cole (*2918*) in 1947: this accident occurred at the Submarine Base, Pearl Harbor, T. H. The man entered the escape tank from the 100-foot lock for ascent; as he passed the 50-foot lock, the attendant observed that the mouthpiece was out of the trainee's mouth. He was ascending rapidly and when he reached the 35-foot level, one of the attendants caught him and compressed his chest region. He was still conscious at that time, but was unconscious when he reached the surface. Within 6 minutes, he was placed in the recompression chamber and taken to a simulated depth of 165 feet. The pulse was rapid and the respiration deep, fast, and stertorous. He remained at 165 feet for 2 hours, during which time he had several convulsive seizures. Phenobarbital was ineffective. Eight hours after he entered the tank, the patient had a very violent convulsion. Spontaneous respiration ceased about an hour later and artificial respiration was given. The pulse was rapid and fairly strong. After another hour the patient had a further convulsion and required restraint. After this the heart began to fail. Caffeine was given in an effort to stimulate respiration but without benefit. The patient was pronounced dead 1 hour later. Death in this case was considered to be due to brain injury from air embolism. Loss of the breathing apparatus was considered to have caused panic with forced closure of the glottis. As the patient rose, the expanding air within the lungs resulted in excessive intrapulmonary pressure which exceeded the strength of the alveolar walls. Rupture of the alveolar walls allowed air to enter the pulmonary vessels and eventually the arterial circulation of the brain.

A case of air embolism occurring at the escape training tank at the Submarine Base, New London, Conn., was reported in 1947 by Hayter (*2919*). The patient was one of a group of 10 men making a free escape from a depth of 35 feet. On the first day of his training, he made 2 escapes from 12 feet, 2 from 18 feet, and 1 from 35 feet. On the final run the patient said he exhaled continuously until the 10-foot level and said he exhaled all he could. From the 10-foot level he swam to the surface. On reaching surface, he collapsed and sank. When he was removed from the water he was unconscious, and pale and bloody saliva was issuing from the mouth. There was gurgling in the throat. The pulse was weak, slow, and regular. Placed in the recompression chamber at a simulated depth of 165 feet, he became conscious, but was confused and appeared to be in mild shock. There was involuntary defecation. Blood pressure was 90/60 mm. Hg. Tendon reflexes, abdominal, and cremasteric reflexes were all absent. Percussion of the chest revealed hyperresonance of the lungs. The region of cardiac dullness was not abnormal. Examination showed subcutaneous emphysema in the supraclavicular fossae

confirmed by X-ray findings. There was no evidence of pneumothorax.

It seems evident that the major hazard in making a free escape arises from inadequate exhalation of air from the lungs. Under such a circumstance positive pressure will be built up within the lungs which may cause the lung tissue to tear, followed either by hemorrhage into the lungs or the forcing of air into the blood stream. Since cases of air embolism have been described from depths as shallow as 10 feet (implying a positive pressure of not more than 4.5 lbs. per sq. in.), it is essential that trainees be taught to exhale during the whole ascent, and enough so that there is never any sense of distention in the chest. Although trainees always express concern as to whether they will have enough air to reach the surface in making free escape, observation of free escapes in many trainees indicates that the air in the lungs is more than adequate to last the subject until he reaches the surface insofar as oxygen content is concerned. Even if he does exhale a bit too much, a few deliberate strokes swimming upward will cause the air in the lungs to expand and fill the chest.

In free escapes under actual operational conditions, a serious potential hazard may be loss of sense of direction in dark water, particularly to negatively buoyant individuals with high specific gravity. It is possible for a man to become disoriented in the water if there is not light above to show or if vision is not sufficiently good to give a reference point. A man may think he is ascending when really he is sinking. One solution to this problem seems to be to take along some buoyant object, such as a pillowcase, a lifejacket, or some other object holding entrapped air.

In escapes made with the aid of the submarine escape apparatus, it is important that the subjects inhale and exhale regularly.

2918. Cole, G. M. Escape training diving accident in the case of Singer, Earl C., StD2, 894–06–15, USN. U. S. Navy. Submarine base, Pearl Harbor, T. H. Report of to Chief, BuMed, 27 March 1947.

2919. Hayter, R. Air embolism in the case of Holst, Richart R., Em3c, 321–96–63, USN. U. S. Navy. Submarine base, New London, Conn. Medical research department. Report of to Chief, BuMed, 30 June 1947, 2 pp.

D. GAS EMBOLISM

Gas in the circulation constitutes a potential hazard not only in lung damage in escape accidents, but also as a part of the picture of decompression sickness. The references give below have been selected as source material for the reader particularly concerned with the mechanism of air embolism in free escape accidents. In this condition, air is forced under pressure into the pulmonary circulation through ruptures in the lung tissue and is admitted into the left heart and thence into the systemic arteries.

For studies of pulmonary air embolism resulting from injection of air on the venous side of the systemic circulation, papers by the following authors may be consulted: Auer and Krueger (*2920*) 1946; Blood and D'Amour (*2925*) 1950; Cameron, De, and Sheikh (*2926*) 1951; and Durant, Long, and Oppenheimer (*2931*) 1947.

Cooper, Marchand, and North (*2927*) 1945 have investigated air embolism from passive overventilation of the rat through a tracheal cannula. Animals received air under pressure sufficient to cause maximal respiratory excursions of the chest and abdomen. They developed multiple hemorragic patches in the lung parechyma, followed by a terminal episode of pulmonary edema with a sudden evolution of pink foam from the trachea. Still greater pressures caused immediate air embolism and death. With each passively overventilated rat, a control animal was anesthetized and cannulated in the same way, but not connected to the air valve. These control animals survived the interval of the experiment by spontaneous respiration through the cannula and exhibited no evidence of lung injury at autopsy. Some degree of overventilation occurred in this control group as a result of operative manipulation of the trachea. There seems little doubt but that these authors have succeded in producing experimentally the conditions responsible for death in free escape accidents.

An early study on cerebral gas embolism reported by Villaret, Cachera, and Fauvert (*2947*) 1937 deserves comment. Working with dogs, these authors concluded that gas emboli in the brain are capable of stopping the circulation in the small vessels. They consider that the air emboli behave as plugs which impede the flow of blood. This provokes a state of temporary ischemia which can last long enough to injure the neurons. The authors stated that they had never observed cerebral vasoconstriction from the flow of gaseous emboli. They consider that the emboli do not act by producing vascular spasm, but believe that the mechanism of injury following air embolism of the brain is cerebral ischemia of simple mechanical origin through gaseous obstruction.

For a report on methods of testing for air embolism, a paper by Karsner (*2937*) 1949 may be consulted. He points out that when air is injected into the dog's superior cava a bubbling sound can be heard through the stethoscope as the air enters

the heart and the same is said to be true of man. The author also discusses the effects of gas bubbles in the brain and cord as a part of the picture of decompression sickness. He points out that if the breath is held during decompression the expansion of air in the lungs may rupture the alveoli so that air enters the tissues to produce interstitial emphysema and may also pass into the blood vessels with consequent air embolism.

In a discussion of the origin and clinical picture of arterial gas embolism in the greater circulation, Rössle (*2943*) 1947 stated that he considered that arterial gas emboli in connection with primary venous air embolism can arise out of passage of the gas through an open foramen ovale or passage of air through arteriovenous anastomoses. He states that air may pass into the arterial circulation in contusion of the lungs through compression of the thorax, through crushing of the lungs "from within" by maximum expansion of the lungs, injection of air by means of a catheter in both men and animals, and through air impact on the lungs in consequence of detonation. He points out that in detonation injuries, gas bubbles are usually found in the coronary arteries and in the base of the brain as well as upper parts of the brain. They are rarely found in the fine mesenteric arteries. Durant (*2930*) 1948 pointed out that arterial gas embolism is commonly associated with localized cerebral or coronary effects. The fact of gas buoyancy determines to a considerable extent the effects of arterial gas embolism in that gas which reaches the aorta will be distributed to those branches which are superiorly located with respect to the trunk. The degree of obstruction of the vessels involved is determined not only by the size of the gas bubbles but also by associated vasospasm induced by the irritant action of the gas in the lumen of the vessel, a view in contradiction with findings of Villaret, Cachera, and Fauvert (*2947*) 1937. Aside from symptoms of pain in the chest, hemiplegia, hemiparesis, hemianaesthesia, monoplegia, nystagmus, convulsions, giddiness, and cyanosis, there may also be observed gas in the retinal vessels. These vessels show pale, silvery sections, representing small columns of air. Durant suggests that in embolism the patient should be placed immediately in a position such that the head is dependent and the trunk is alined midway between the left lateral and prone positions. He considers that this position minimizes the amount of gas reaching the cerebral and coronary arteries.

Cerebral air embolism from air entering the pulmonary venous circulation has also been described by Hare (*2935*) 1949. He has drawn attention to the early signs of cerebral air embolism consisting of vertigo and pallor, followed by cyanosis and respiratory difficulty, loss of consciousness, sharp drop in blood pressure, bradycardia, apnea, convulsions, urinary and fecal incontinence, focal neurological disturbances, and, in some instances, death. Courville (*2929*) 1945 has drawn attention to the fact that marked cerebral symptoms or sudden death from air embolism are usually due to an overwhelming invasion of air into the pulmonary veins as in injuries to the chest and lungs in pulmonary operations.

Rössle (*2944*) 1949 has described several cases of arterial gas embolism in which the patients survive for periods varying from several hours to several days. This paper describes in detail the histological findings in the cerebral vessels. The cerebral capillaries are dilated, and air penetrates into the perivascular spaces. There is also penetration of air into the glial tissue and the pericellular spaces of ganglion cells. There are small necrobiotic areas in the cerebral tissue and small hemorrhages.

The management of cases of escape accident includes immediate placing of the head in the dependent position and carrying the victim in this position at once to the recompression chamber when this is available. The patient should remain in the head-down, feet-up position as for shock during and after rapid recompression to a simulated depth of 165 feet. Convulsions and other symptoms must be treated as they arise.

For other studies on gas embolism, papers by the following authors should be consulted: Barach (*2923*) 1948; Binet and Burstein (*2924*) 1947; Gt. Brit. Medical Research Council (*2932*) 1947; Leriche (*2939*) 1947; Milwidsky (*2940*) 1948; Neuhof (*2941*) 1948; Whitteridge (*2948*) 1951; and Zilliacus (*2949*) 1946.

2920. Auer, J. and H. Krueger. Accidental air embolism and fibrin formation in the heart of rabbit. *Proc. Soc. exp. Biol., N. Y.*, 1946, *61:* 166–169. [P]

2921. Bageant, W. E. and L. A. Rapee. The treatment of pulmonary embolus by stellate block. *Anesthesiol.*, 1947, *8:* 500–505. [CH]

2922. Baker, D. V., Jr., R. Warren, J. Homans, and D. Littman. Pulmonary embolism. Evaluation of a policy for prophylaxis and therapy. *New Engl. J. Med.*, 1950. *242:* 923–928.

2923. Barach, A. L. Pulmonary embolism and infarction. pp. 215–217 in *Physiologic therapy in respiratory diseases*. Second edition, Philadelphia. J. B. Lippincott Co., 1948, 408 pp.

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2925. Blood, F. R. and F. E. D'Amour. Cardiac output in the rat and its relationship to air embolism. *Fed. Proc. Amer. Soc. exp. Biol.*, 1950, *9:* 13.

2926. Cameron, G. R., S. N. De, and A. H. Sheikh. Cardio-vascular responses to air embolism. *J. Path. Bact.*, 1951, *63:* 181–194.

2927. Cooper, M. R., J. F. Marchand, and N. North. Carbon dioxide depletion and air embolism from passive overventilation of the rat by tracheal cannula. U. S. NRC–CAM. *C. A. M. rept. no. 478,* 4 October 1945, 4 pp.

2928. Cort, J. H. and G. D. Davis. Observations on the role of vagal activity in the effects of pulmonary embolism. *Yale J. Biol. Med.*, 1950, *22:* 213–218. [P]

2929. Courville, C. B. Diseases of the intracranial and intraspinal blood vessels. pp. 87–148 in: *Pathology of the central nervous system.* Mountain View, California. Pacific Press Publishing Association, 1945. 450 pp.

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2931. Durant, T. M., J. Long, and M. J. Oppenheimer. Pulmonary (venous) air embolism. *Amer. Heart J.*, 1947, *33:* 269–281. [P]

2932. Gt. Brit. MRC–RNPRC, UPS. Minutes of the 25th meeting of the underwater physiology subcommittee. *R. N. P. 47/365, U. P. S. 80,* 23 April 1947, 3 pp.

2933. Groedel, F. M., B. Kisch, and M. Miller. Electrocardiographic changes following air embolism in man. *Exp. Med. Surg.*, 1949, *7:* 73–77. [CH]

2934. Hara, M. and J. R. Smith. Experimental observations on embolism of pulmonary lobar arteries. *J. thorac. Surg.*, 1949, *18:* 536–542. [P]

2935. Hare, C. C. Cerebral air embolism. pp. 683–685 in: *Injuries of the brain and spinal cord and their coverings.* Edited by Samuel Brock. Third edition. Baltimore. The Williams & Wilkins Co., 1949, 783 pp.

2936. Haynes, F. W., T. D. Kinney, H. K. Hellems, and L. Dexter. Circulatory changes in experimental pulmonary embolism. *Fed. Proc. Amer. Soc. exp. Biol.*, 1947, *6:* 125–126. [P]

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2939. Leriche, R. *Les embolies de l'artère pulmonaire et des artères des membres. Physiologie pathologique et traitement.* Paris, Masson & Cie, 1947, 126 pp. [R]

2940. Milwidsky, H. Therapeutischer Paravertebral-Block des Sympathicus bei peripherer arterieller Embolie. *Schweiz. med. Wschr.*, 1948, *78:* 301–302. [CH]

2941. Neuhof, H. *Venous thrombosis and pulmonary embolism.* New York. Grune & Stratton, 1948, 159 pp.

2942. Pratt, C. L. G. and H. J. Taylor. The risk of bends or vascular embolism during simulated escapes from (a) 300 ft. (b) 150 ft. Gt. Brit. MRC–RNPRC, UPS. *R. N. P. 47/347, U. P. S. 78,* January 1947, 5 pp.

2943. Rössle, R. Ursachen und Folgen der arteriellen Luftembolien des grossen Kreislaufes. *Virchows, Arch.*, 1947, *314:* 511–533. [R] [CH]

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2946. Stallworth, J. M., J. B. Martin, and R. W. Postlethwait. Aspiration of the heart in air embolism. *J. Amer. med. Ass.*, 1950, *143:* 1250–1251. [CH]

2947. Villaret, M., R. Cachera, and R. Fauvert. L'embolie gazeuse cérébrale; ses effets circulatoires locaux. *C. R. Soc. Biol., Paris,* 1937, *125:* 108–111.

2948. Whitteridge, D. Multiple embolism of the lung and rapid shallow breathing. *Physiol. Rev.*, 1950, *30:* 475–486. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 881.

2949. Zilliacus, H. On the specific treatment of thrombosis and pulmonary embolism with anticoagulants, with particular reference to the post-thrombotic sequelae. *Acta med. scand., Suppl.*, 1946, *171:* 221 pp. (French, German and Russian summaries.) [R; P]

IX. SPECIAL DIVING ACCIDENTS

Divers are subject to certain special accidents including "blowing up," "squeeze," and underwater confinement. The accidents known as "blowing up" and divers' "squeeze" have been described in the first volume of this Sourcebook (pp. 228–230). Under certain circumstances, the diver may be forced rapidly to the surface because of filling of the diving dress with air. These accidents ("blowing up") are associated with acute manifestations of decompression sickness. Cases have been described of almost immediate death from too rapid surfacing. For consideration of special accidents to divers, papers by Buyard (*2950*) 1946 and U. S. Navy, BuNavPers (*2954*) 1949 should be consulted.

As a diver descends, the air pressure within the helmet and the suit must be correspondingly increased with the increasing pressure of the column of water against the body surface. At any depth, the air pressure within the helmet in the suit must be maintained. If the pressure within the helmet suddenly falls or if the hydrostatic pressure on the outside of the body increases suddenly without a corresponding increase in the air pressure within the helmet, a differential pressure is created which interferes with respiration and drives blood into the head and neck or may even force portions of the body itself up into the helmet. This condition, known as divers' "squeeze," occurs if a diver falls off a ledge on the bottom to a new level without a corresponding increase in helmet pressure. Roer (*2952*) 1948–49 has given an excellent and complete review of divers' "squeeze," including a comprehensive bibliography and some very complete case histories. Three autopsy reports are included. The author has also provided experiments on rabbits subjected to "squeeze." The minimum depth at which the condition may become fatal is 1.40 meters in the lying-down position and about 3 meters standing up, corresponding to a suction of 100 mm. Hg within the helmet-lung area. In fatal cases of divers'

"squeeze," there is always, according to the author, emphysema of the skin.

Three cases of underwater confinement have been described by Romney (*2953*) 1946. The first was that of a 26-year-old qualified deep-sea diver, working beneath a sunken LST, who was trapped for 72 hours at 55 feet of water. There were no symptoms of compressed-air illness. When the diver was examined on being brought finally to the surface, he was alert, calm, cooperative, and physically exhausted. He was recompressed to 100 feet simulated depth for 30 minutes, decompressed, and later hospitalized. The second case was that of a 24-year-old qualified deep-sea diver who was working with the diver just described. He became excited and frantic. It is stated that he became disoriented and irrational, and lost telephonic contact. When he was brought to the surface 75 hours after descent, his suit and helmet were found to be intact and contained an adequate air supply. This man did not survive. The third case was that of a 36-year-old qualified diver who went to rescue the two previous divers. Another cave-in trapped him for 17 hours at a depth of 45 feet. A modified type of surface decompression was employed. The subject was cooperative, but extremely tired. He recuperated within 2 weeks. It was assumed and seems probable that the fatal outcome in the second case was due in part to intense emotional stress.

For a report on the circumstances, opinions, and recommendations in connection with further diving accidents, papers by Van der Aue (*2955*) 1949 and Dietrich, Behnke, and McDonald (*2951*) 1949 should be consulted.

2950. Buyard, P. Guide thérapeutique des scaphandriers. *Rev. Méd. nav.*, 1946, *1:* 267–284. [D]

2951. Dietrich, W. F., A. R. Behnke, and J. H. McDonald. The proceedings, findings of facts, opinions and recommendations of the board of investigation in the case of death of Egnacio Lopez Huerta, 381–34–88, chief metalsmith. U. S. Navy. Naval gun factory, EDU. 3 June 1949, 75 pp.

2952. Roer, H. Ueber das Blaukommen der Taucher (Morbus caerulescens). *Dtsch. Z. ges. gerichtl. Med.*, 1948/49, *39:* 378–420 [CH] [R] [P]

2953. Romney, S. L. Underwater confinement—report of three cases. *Nav. med. Bull., Wash.*, 1946, *46:* 1259–1264.

2954. U. S. Navy. BuNavPers. Surface decompression procedure. pp. 118–132 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp. [CH] [D]

2955. Van der Aue, O. E. Diving accident in the case of Huerta, Ignacio L., MEC, 381–34–88, U. S. Navy. Naval gun factory, EDU. Report to Chief, BuMed. 6 March 1949, 6 pp.

X. BLAST INJURIES

Underwater blast constitutes an important problem to the underwater swimmer, deep-sea diver, and survivor of disaster at sea. During World War II, underwater blast was a far greater cause of casualties than air blast. Detonation of armed charges on a sinking vessel, accidental explosion of mines, or countermeasure explosions by the enemy are a constant threat to the buoyant or submerged swimmer.

It is not intended under this heading to include in its entirety the literature on air blast. The reader should consult reports such as those by Baron (*2956*) 1948, Burnett (*2960*) 1948, Corey and Gersh (*2968*) 1944, Friedman (*2970*) 1948, Ruskin and Beard (*2975*) 1948, and Smith (*2976*) 1949. Reference should be made to an excellent review on blast published in 1949 by Clemedson (*2964*).

Martin (*2973*) 1943 describes a case of rectal perforation resulting from immersion blast. A 28-year-old seaman was swimming in the water following the torpedoing of his ship, while destroyers made depth-charge attacks on the submarine. Examination of the survivor 14 hours later revealed no external bruises or fractures. A small amount of blood had been passed from the anus. His temperature was 100° F. and his pulse was 120. Abdominal rigidity was present, especially over the right iliac fossa. Laparotomy following saline and glucose infusion revealed pus in the peritoneal cavity and a 1-cm. laceration on the anterior surface of the rectum. The perforation was oversewn and buried with a pursestring suture. After draining the pelvis, the abdomen was closed and 2 pints of blood administered. The following day the patient exhibited jaundice, and on the third day he presented a paralytic ileus accompanied by vomiting and a pulse of 140. Duodenal drainage, intravenous saline drip, and morphine administration were of no avail. The patient died 52 hours after the operation. Autopsy showed a general peritonitis having originated in the pelvis. The paralytic ileus involved the whole left bowel; the right lung showed a contusion on the anterior surface near the medial and inferior borders.

For detailed studies of immersion injuries, the reader is referred to the section on water or immersion blast injuries in Submarine Medicine Practice (*2977*) 1949. A description is given of cases admitted to the Pearl Harbor Naval Hospital from the naval battle near Midway Island. Approximately 5 days had elapsed between the battle and arrival at the hospital, and out of the group of 33 admitted to the hospital, over half walked in and required very little definite treatment. The mortality rate was very high for those seriously injured. The characteristic finding for the seriously injured group as a whole was a distended and silent ab-

domen. Those critically ill on arrival presented a picture of intestinal obstruction of the adynamic or paralytic type. In several there was a superimposed general peritonitis. Roentgenograms revealed free gas beneath the diaphragm in two cases. In one of these instances the patient was moribund and died within a few hours following admission. A Levin or Miller-Abbott tube was introduced in all bed-ridden patients, and fluids including 5 percent glucose, electrolytes, vitamins, and blood plasma were given generously by vein. All received intravenous sulfadiazine in amounts sufficient to maintain a concentration of 15 mg. per 100 cu. cm. of blood. Surgery was resorted to in only two cases in this entire group. All except two of those having post-mortem examination showed one or more perforations of the bowel with general peritonitis. The majority of these perforations were through localized necrotic areas in the jejunum or ileum. In one, there were two perforations in the large bowel in addition to one or more in the small intestine. In one patient perforation was demonstrated, but his cecum and ascending colon were a formless, hemorrhagic, necrotic mass. It is stated that the severity of injury from immersion blast depends upon several factors: (1) proximity to the blast; (2) intensity of the blast; (3) whether almost completely submerged or only partially submerged; (4) whether swimming on the stomach or on the back; and (5) whether the thoracic and abdominal areas are protected by a life jacket. It appears that the underwater concussion wave produces tissue injury by *shredding* the tissue as it passes from a solid to a gaseous medium within the body. With the body in the supine position in the water or protected over the thorax and abdomen by kapok or foam rubber, the injurious effects of the compression wave may be minimized.

According to Clemedson (*2963*) 1948, animals exposed to underwater blast are more severely injured when they are immersed 1 meter below the water's surface than when floating on the surface. Death in rabbits seemed to be due to suffocation by extensive pulmonary hemorrhages and blood clots in the respiratory tract. The usual lesions of the abdominal viscera were seen, and in the more severe cases a diffuse edema in the mucosa and submucosa of the gut was noted. The gut exhibited maximal contraction and, when squeezed, felt like a tendon.

An experimental study of physical and subjective sensations of deep-sea divers and underwater demolition team members exposed to blast was carried out by Corey (*2967*) 1946. The divers acting as subjects were subjected to concussion from charges of 1 to 300 pounds in weight. It was found that divers can tolerate calculated explosion pressures up to 50 lbs. per square inch without serious discomfort or injury. During the work performed on the stage in deep water, the divers' heads were at times thrown with different degrees of violence against portions of the helmet and breastplate, but in no instance was the blow to the head of sufficient violence to break or bruise the skin or render the subject dizzy or unconscious, or to interfere in any way with prompt mental or physical reactions. To determine lethal blast pressures, strips of beef intestine were suspended inside a diving dress, at the level corresponding to the umbilicus, by means of a weight and a cord attached to the chin valve of the helmet. The suit was then lowered into the water and exposed to blasts from 114-pound charges. The calculated pressure at which rupture of the intestinal sample occurred was considered "lethal." From the results of the experiment, the author concluded that a calculated underwater blast pressure of 300 lbs. per square inch may be considered lethal for divers wearing standard deep-sea diving dress. It was found that the British anti-blast vest offered a measure of protection against underwater concussion, the "lethal" pressure being raised to at least 525 lbs. per square inch.

Corey also exposed underwater swimmers to blast from 110-pound demolition charges. Six men wore swimming trunks, and one of these wore, in addition, an inflatable lifebelt, while four were equipped with the standard Navy kapok lifejacket. The water was 5 feet deep over a soft mud bottom, and the charges were detonated at a depth of 3 feet with the men immersed to the neck. The underwater concussion produced definite abdominal sensations at rather low pressures (22.5 lbs. per square inch), but no impact of the shock wave against the thorax could be detected. It was concluded that calculated explosion pressures up to 70 lbs. per square inch may be readily tolerated in shallow water.

Draeger, Barr, and Sager (*2969*) 1946 state that underwater blast pressures over 250 lbs. per square inch will result in intestinal perforation. Because the body has a density approximately equal to water, only air-containing portions of the body are subjected to sudden compression and expansion, causing a rupture of tissues adjacent to the contained air. The authors recommend that the patients be treated for shock and given bed rest. Handling and excessive transportation should be avoided. Fluids should be given to maintain the electrolyte balance and a Miller-Abbott tube should be used in cases of paralytic ileus.

The reader is advised to consult reports by Benzinger (*2958* and *2959*) 1950–51 for an excellent discussion of the mechanics and physiological effects of air and water blast. Arterial air embolism, caused by rupture of the boundaries between alveolar spaces and alveolar capillaries, was shown in dogs to be the chief cause of death from blast in air as well as under water. Cerebral focal symptoms were found when the head of the animal was protected from the blast, while its trunk was exposed. With the head exposed and the trunk shielded, cerebral focal symptoms were not observed. Post-mortem examination revealed aïr emboli in the cardiac and cerebral arteries. It thus appears that the cerebral symptoms arose from air emboli reaching the brain from the exposed trunk areas.

According to Clemedson and Granstom (*2965*) 1950, lung hemorrhages and rib markings are the result of tearing forces produced by pressure differences between the lungs and the pleural space. These pressure differences are stated to be due to different accelerations of the structural thoracic elements. The risk of tearing is expected to be greatest in those parts of the lung which correspond to the costal interspaces, and that is where the rib markings were observed in the experimental animals.

Protection of divers against underwater explosions is outlined in a report by the Great Britain Medical Research Council (*2972*) 1945. It is stated that the intensity of damage to the diver from underwater blast may be reduced if the diver wears a kapok garment surrounding his chest and abdomen. It is recommended that a shockabsorbing headdress be worn inside the rigid helmet. Protection afforded by kapok jerkins is based on the layer of air held within the kapok, the efficiency of the kapok being reduced if it becomes wet or soggy. Wearing kapok jerkins has been shown to protect a man from peak pressures up to 225 lbs. per square inch. A momentary discomfort may be experienced at peak pressure.

For other general reports on underwater blast, the reader may consult articles by Bebb (*2957*) 1951, Cameron (*2962*) 1947, Cole (*2966*) 1948, Gala (*2971*) 1947, Netter (*2974*) 1948, U. S. Navy (*2978*) 1950, Wright (*2979*) 1947, and Young (*2980*) 1945.

2956. Baron, S. H. The repair of the eardrum in blast injuries. *Ann. Otol., etc., St. Louis,* 1948, *57:* 143–152. [CH]

2957. Bebb, A. H. Underwater blast injury—some physical factors. Gt. Brit. MRC–RNPRC, UWB. Royal naval physiological laboratory, Alverstoke, Hants. *R. N. P. 51/641, U. W. B. 22,* January 1951, 11 pp.

2958. Benzinger, T. Physiological effects of blast in air and water. pp. 1225–1259 in: *German aviation medicine World War II. Vol. II.* Department of the Air Force, Washington, D. C., 1950, 1302 pp. [R]

2959. Benzinger, T. Causes of death from blast. *Amer. J. Physiol.,* 1951, *167:* 767. Abstr.

2960. Burnett, H. A. Early evaluation of blast injury. *Milit. Surg.,* 1948, *103:* 275–278. [CH]

2961. Cameron, G. R. A survey of the effects of underwater blast on human beings and animals. Gt. Brit. MRC–RNPRC, UWB. *R. N. P. 47/380, U. W. B. 4,* September 1947, 4 pp.

2962. Cameron, G. R. Summary of literature on the effects of underwater blast on human beings and animals (1940–47). Gt. Brit. MRC–RNPRC, UWB. *R. N. P. 47/381, U. W. B. 5,* September 1947, 23 pp. [R]

2963. Clemedson, C. J. Om undervattensdetonationsskador [Immersion Blast Injuries]. *Tidskr. milit. Hälsov.,* 1948, *73:* 1–34.

2964. Clemedson, C. J. An experimental study on air blast injuries. *Acta physiol. scand.,* Suppl., 1949, *61:* 1–200. [P]

2965. Clemedson, C. J. and S. A. Granstom. Studies of the genesis of "Rib markings" in lung blast injury. *Acta. physiol., scand.,* 1950, *21:* 131–144. [P]

2966. Cole, R. H. *Underwater explosions.* Princeton, Princeton University Press, 1948, 437 pp. [D]

2967. Corey, E. L. Medical aspects of blast. *Nav. med. Bull., Wash.,* 1946, *46:* 623–652. [R]

2968. Corey, E. L. and I. Gersh. Observations on the effects of air blast on the central nervous system and viscera of cats and rabbits. U. S. Navy. NMRI. *Project X–219,* 24 June 1944, 4 pp. [P]

2969. Draeger, R. H., J. S. Barr, and W. W. Sager. Blast injury. *J. Amer. med. Ass.,* 1946, *132:* 762–767. *J. industr. Hyg.,* 1947, *29:* abstract section: 38–39. [R]

2970. Friedman, O. Blast injuries of the ears. *Arch. Otolaryng., Chicago,* 1948, *47:* 471–484. [CH]

2971. Gala, P. Syndrome des phénomènes d'explosion. *Rev. Méd. nav.,* 1947, *2:* 31–50. [D]

2972. Gt. Brit. MRC–RNPRC, UWB. Protection of divers against underwater explosions. *R. N. P. 47/374, U. W. B. 1,* 1 November 1945, 6 pp.

2973. Martin, P. G. C. Perforation of rectum from immersion blast. *Lancet,* 1943: *II:* 605–606. [CH]

2974. Netter, Frank H. Immersion blast injuries of the abdomen. pp. 153 in: *The Ciba collection of medical illustrations.* Ciba Pharmaceutical Products, Inc., Summit, N. J., 1948, 222 pp.

2975. Ruskin, A. and O. W. Beard. The Texas City disaster—cardiovascular studies, with followup results. *Tex. Rep. Biol. Med.,* 1948, *6:* 234–259. [CH]

2976. Smith, H. E. Accommodative defect following atmospheric concussion. *Amer. J. Opthal.,* 1949, *32:* 959–966. [CH]

2977. U. S. Navy. BuNavPers. Water or immersion blast injuries. pp. 55–68 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp. [CH] [D]

2978. U. S. Navy, Naval medical school, Bethesda, Md. Blast injury. pp. 176–177 in: *Color atlas of pathology.* Philadelphia, J. B. Lippincott Co., 1950, 546 pp. [CH]

2979. Wright, H. C. Subjective effects of distant underwater explosions. Gt. Brit. MRC–RNPRC, UWB. *R. N. P. 47/375, U. W. B. 2,* April 1947, 25 pp.

2980. Young, M. W. Mechanics of blast injuries. *War. Med., Chicago,* 1945, *8:* 73–81. [R] [P]

XI. DROWNING

The danger of drowning in submariners, divers, and caisson and tunnel workers is probably greater than in other occupations, but because of the general nature of this particular subject it is recommended that the reader consult standard works on medicine and occupational diseases. The section on resuscitation and respiratory devices (p. 290) includes information pertaining to resuscitation from drowning, while the data presented here are concerned primarily with the physiological and biochemical events transpiring during drowning.

Swann, Brucer, Moore, and Vezien (*2985*) 1947 conducted drowning experiments on 8 healthy dogs under local procaine anesthesia. Drowning was accomplished by flooding a sealed face mask with fresh or salt water. Blood oxygen was found to drop to zero within 3 minutes after the beginning by water inhalation, but the carbon dioxide, after a transitory rise, fell again to the normal range. The pH declined to approximately 7.1. During fresh-water drowning there was an abrupt hemodilution, indicated by a rapid drop in plasma protein, hemoglobin, and chloride. In sea-water drowning, hemoconcentration occurred. During fresh-water drowning, ventricular fibrillation occurred in 4 out of 6 dogs after 3 to 5 minutes of submersion. Fibrillation was not observed in any of the dogs drowned in sea water.

Franko (*2981*) 1949 subjected anesthetized rabbits to drowning by pouring water or Ringer's solution down the trachea. Circulation and respiration ceased most rapidly when the water at 20° C. was used. Dilution of arterial blood was rapid and powerful. Vagotomy, atropine injection, 38° C. water, or pregnancy slightly lengthened the time of survival. The author presumed that the injurious effects of water in the lungs are in principle due to the following factors: (1) prevention of external interchange of gases by liquid in the respiratory tract; (2) hydremia caused by absorbed water; (3) osmotic injuries in the lung tissue; and (4) the possible liberation of substances capable of decreasing the blood pressure.

Anesthetized and unanesthetized rats drowned by submersion demonstrated four respiratory phases before cessation of respiratory movements. Gray (*2982*) 1951 describes these phases as: (1) a short period of apnea; (2) a period of dyspnea; (3) a long period of anoxic apnea; and (4) a short series of respiratory movements of about the amplitude of normal respirations, but accompanied by neck and facial movements. Rats submerged in water at 1.0° C. reached the beginning of the fourth phase in about 155 seconds, while in water at 40° C. the time required was approximately 95 seconds. The time of survival increased further as the temperature was raised to 55° C., and then decreased at higher temperatures. A report by Veen (*2986*) 1947 states that following the submersion of dogs in water, the volume of air remaining in the lungs decreased to approximately 107 cu. cm.

Changes observed in the lungs and liver following drowning are reported by Shkaravskii (*2983*) 1949. In all cases observed, the fundamental argyrophil substances in the lungs and liver outlast the phases of dilution. The dilution of the fundamental argyrophil substances occurs quickly, even in the short-duration drownings observed in human and in experimental animals. The quick onset of lung and liver edema during drowning was attributed to increased permeability of the filtering membranes.

2981. Franko, O. and A. Vartiainen. Effects of intratracheally poured water on blood pressure and respiration in rabbit, with reference to the pathologic physiology of drowning. *Ann. Med. exp. Fenn.*, 1949, *27:* 110–127. [P]

2982. Gray, S. W. Respiratory movement of rat during drowning and influence of water temperature upon survival after submersion. *Amer. J. Physiol.*, 1951, *167:* 95–102. [P]

2983. Shkaravskii, F. I. Izmenenie osnovnogo argirofilnogo veshchetva v legkikh i pecheni pri utoplenii. [Changes of fundamental argyrophil substances in the lungs and in the liver after drowning.] pp. 288–293 in: *Gipoksiia,* Kiev, Akad Nauk. Ukr. SSR., 1949, 415 pp.

2984. Swann, H. G. and M. Brucer. The cardiorespiratory and biochemical events during rapid anoxic death. VI. Fresh water and sea water drowning. *Texas Rep. Biol. Med.*, 1949, *7:* 604–618. *Abstr. World Med.*, 1950, *8:* 230.

2985. Swann, H. G., M. Brucer, C. Moore, and M. L. Vezien. Fresh water and sea water drowning: a study of the terminal cardiac and biochemical events. *Texas Rep. Biol. Med.*, 1947, *5:* 423–437. [P]

2986. Veen, H. The air content of the lungs after drowning. *Arch. neerl. Physiol.*, 1947, *28:* 451–461 [P]

XII. SPECIAL PROBLEMS OF SNORKEL

In 1945, Hayter and Bateman (*2992*) reported observations made during simulated snorkel operations carried out at Portsmouth Navy Yard aboard the U. S. S. *Sirage* (*SS 485*) in September of 1945. At no time did the drop in barometric pressure approach levels dangerous to human life. The highest carbon monoxide concentration was only 0.002 percent, which may be considered to be of no importance. The tests demonstrated that submergence of the snorkel head for 45 seconds will not cause a dangerous drop in barometric pressure. Cycling operations in which the head valve is closed up to two-thirds of the time will reach pressure equilibrium at a safe pressure if the cycles are of short duration. Submergence of the snorkel head

for over 2 minutes will produce less of a reduction in pressure than that found at an altitude of 10,000 feet. The incidence of aerotitis media encountered among personnel involved in these tests was high and indicated to the authors the need for further study along this line. It was noted that the conditions of the experiment were more severe than would probably be encountered in actual snorkel operations. The 19 men aboard were examined with an otoscope. Ten ears in eight men showed evidence of mild aerotitis media (grades 1 and 2), and one man had severe bilateral aerotitis media. The authors believed that the large number of involved ears encountered in these tests was due primarily to the sudden rise in barometric pressure encountered when the engines shut off.

In 1947, Hayter (*2991*) gave a medical report on snorkel operations in the U. S. S. *Amberjack* (SS–522). The observations recorded in this report were made during two periods of snorkeling, one lasting 55½ hours and the other 40 hours. The fluctuation of barometic pressure was usually 1 to 2 in. of Hg. Sleep was undisturbed by snorkeling under the conditions of these observations. During one period there was sufficient pain to awaken personnel when at the request of the medical officer maximum pressure fluctuations were produced. At this time, personnel showed redness of the eardrums. Ventilation of the boat during snorkeling was found to be adequate. In 1947, a report was given by Bateman, Hayter, Haines, and Cook (*2987*) of a preliminary study of the medical aspects of snorkel operations carried out on American personnel manning the captured German submarine, *U–873*. Fifty-six American crew members were involved in the study. There were 4 days of snorkeling divided into two sessions a week apart. The short period of operations and the limited number of subjects, as well as the differences between this submarine and those to which snorkels might be adapted prevents, according to the authors, any final, clear-cut answers to the many problems associated with snorkel operations. It was found that the pressure variations were usually less than 1 in. of Hg during ordinary snorkeling, and personnel soon became accustomed to the constant pressure variations. During simulated loss of depth control, the pressure dropped to 18.5 in. of Hg (equivalent to an altitude of 12,400 feet) in a period of 4½ minutes. The most rapid rise in pressure recorded during the return of pressure to normal was at a rate of 0.1 in. of Hg per second (average, 0.03 in. of Hg per second). The limiting factor during simulated loss of depth control was the presence of exhaust fumes in the engine room. The highest carbon monoxide concentration there at these times was 4.7 parts per 10,000. The irritant character of the fumes was such that exposure for more than a short time could not be tolerated. In these studies, 40 percent of the personnel developed aerotitis media of grade 2, 3, or 4. Grade 4 ears with free bleeding into the middle ear were present in 16 percent of the subjects. The same incidence and severity of ear damage was encountered in ordinary snorkel operation as in simulated loss of depth control. During ordinary snorkel operations, no pain was associated with the damage and there was no apparent awareness of it, whereas during simulated loss of depth control it was necessary voluntarily to clear the ears. Some subjects with colds complained of moderate pain. In the subjects of these tests, the presence or absence of aerotitis media during the first snorkel session was a valid predictor of the presence or absence of aerotitis media during the second session. Administration of the routine 50-lb. pressure test did not satisfactorily predict the occurrence of aerotitis media during snorkeling. The authors stated that in this regard more observations were necessary to determine the need for changing the test procedure in the selection of personnel for snorkel operations. A higher than ordinary incidence of aerotitis media was encountered in those personnel who slept during the snorkel operations (63 percent in the sleeping group as compared with 29 percent in the waking group), and those who were suffering from cold (66 percent in those with colds as compared with 31 percent in controls). No nausea, dizziness, or diarrhea were experienced by any of the crew, although these effects have previously been ascribed to snorkeling in the German reports. Subsequent experiences with snorkeling in the U. S. Navy and in the British Navy have revealed that aerotitis media is not a special hazard of normal snorkeling operations.

Schaefer (*2994*), describing German operations in 1948, drew attention to periodic pressure drops of 200 and 300 millibars recorded within short intervals. He also reported middle-ear damage and defects of hearing in submariners in snorkel submarines. In discussing fluctuating atmospheric pressures under trial conditions with British prototype snorkel equipment, Ellis (*2989*) 1949 found no evidence to suggest that special conditions will occur in snorkel-fitted submarines to influence adversely the health or efficiency of the crews. Reporting in 1949, Davidson (*2988*) found that carefully selected submariners experienced no special ear problems in snorkel submarines; in fact, hearing improved in some cases.

The effect of prolonged snorkeling on the health of officers and men and on the general habitalibity of the submarine has been a subject which has engaged the attention of submarine surgeons. Ritch (*2993*) 1948 has described medical aspects of a cruise of the guppy-snorkel submarine U. S. S. *Trumpetfish* (SS–425), in which the submarine was submerged for 330 hours. Of this time, 309 hours were spent in snorkeling. Pressure fluctuations within the submarine of sufficient magnitude to require equalization within the middle ear occurred only during relatively short periods of time of the snorkel cruising. During the cruise, seven men exhibited tympanic membrane trauma visible on otoscopic examination. Ritch discussed the following problems which may be enhanced in guppy-snorkel submarines: (1) boredom and tendency toward apathy of personnel; (2) general overcrowding, particularly in berthing facilities; (3) ventilation problems; (4) air-conditioning problems; (5) problems of fresh-water distillation and sewage disposal; and (6) problems of garbage and refuse disposal. In these studies, 48 percent of the personnel reported that their ears were cleared automatically. Fifty-two percent of the men complained of some disturbance of sleep. Men with head colds experienced moderate to severe headaches associated with the pressure fluctuations. It was expected by the author that snorkeling in heavy seas would raise the percentage of ear trauma.

Willmon and Ritch (*2995*) 1948 have reported on the general health and morale of officers and crew during a 30-day simulated war patrol aboard the U. S. S. *Irex* (SS–482). The U. S. S. *Irex,* an experimental snorkel submarine with conventional superstructure, was on patrol during the period from 1 to 30 March 1948 during which time she was submerged for 615 hours: 390 by snorkel and 225 on battery propulsion. During this patrol the morale and health were good. The authors considered that the increased monotony and emotional stress incident to a largely or totally submerged patrol makes mandatory an even more stringent personnel selection program and efforts toward increased physical and emotional comfort, proper illumination, pleasing interior color and design, and all diversions that may be practical. The effect on personnel of atmospheric pressure fluctuation due to opening and closing of the snorkel head valve presented no problem during this patrol. However, the conditions of operations were not considered to afford a critical evaluation of the problem in that only negligible pressure fluctuations were experienced. The authors emphasized the importance of an appraisal of the effect on personnel of prolonged snorkeling during periods of sleep, and recommended that this could be most easily accomplished by a proposed dockside study.

Reference may also be made to a British commentary on problems of motion and time study in snorkel-fitted submarines (*2990*).

2987. Bateman, J. G., R. Hayter, H. L. Haines, and N. L. Cook. A preliminary study of the medical aspects of schnorchel operations. U. S. Navy. BuMed., *Project X–606* (*Sub 131*), 15 January 1947, 23 pp. [M]

2988. Davidson, W. M. Physiological problems in snort-fitted submarines. *J. R. nav. med. Serv.,* 1949, *35:* 26–29. [R]

2989. Ellis, F. P. Fluctuating atmospheric pressures. A novel environmental variant observed in submarines. *Brit. J. industr. Med.,* 1949, *6:* 24–30. [M]

2990. Gt. Brit. MRC–RNPRC, OES. Notes on a meeting to discuss problems of motion and time study in snort-fitted submarines. *R. N. P. 48/464, O. E. S. 151,* 5 July 1948, 5 pp.

2991. Hayter, R. Medical report on snorkel operations of U. S. S. *Amberjack* (SS–522) U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 002 009* (*X–753, Sub. no. 156*), *Interim rept. no. 1,* 16 December 1947, 7 pp.

2992. Hayter, R. and J. G. Bateman. Observations made during simulated Schnorchel operations carried out at Portsmouth Navy Yard aboard the U. S. S. *Sirage* (SS–485) on 11, 12, and 13 September 1945. U. S. Navy. NMRI. *Interim report, Project X–605 and X–606,* 1 November 1945, 6 pp.

2993. Ritch, T. G. Report on the effects of prolonged snorkeling on the health of the officers and men and on the general habitability of the guppy-snorkel submarine U. S. S. *Trumpetfish* (SS–425). U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 002 009* (*X–753, Sub. no. 156*), *Rept. no. 2,* 12 April 1948, 9 pp.

2994. Schaefer, K. E. Technical influences. IV. Air-pressure. Pp. B: I–56—B: I–59 in: *Monograph on submarine medicine,* Folio I, Germany. U. S. Zone. Office of naval advisor. 1948.

2995. Willmon, T. L. and T. G. Ritch. The general health and morale of the officers and crew during a 30-day simulated war patrol aboard a snorkel submarine. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 009, Rept. no. 3,* 4 November 1948, 8 pp.

XIII. DENTAL PROBLEMS

The problem of dental pain is one of particular concern not only in divers but also in aviators. Susceptibility to the traumatic effects of pressure changes on oral tissues depends primarily on a hyperemic pulp, pulpitis, or necrosis of the pulp. Exposure by Orban (*2999*) 1945 of dogs decompressed to a simulated altitude of 38,000 feet after their teeth had been test filled with amalgam, cement, cilicate, zinc oxide and cugenol, and croton oil, showed no pathological changes in the teeth. One dog sacrificed at altitude and with the teeth fixed at altitude showed blood vessels surrounded by

polymorphonuclear leukocytes. Another dog sacrificed in the chamber revealed extensive hyperemia in the pulp with some microscopic bleeding. Additional studies by Orban, Ritchey, and Zander (*3000*) 1945 on asphyxiated dogs revealed hyperemia and hemorrhage in all teeth checked; both conditions were more or less independent of the cavity preparation or the use of croton oil. The control teeth showed similar findings.

Kennon and Osborn (*2996, 2997*) in 1945 ascribed pain in the oral tissue during decompression or recompression to imperfect ventilation of the maxillary sinuses. Usually the pain was felt in the upper bicuspids or the first or second molars, the pain being sporadic or constant but not localized in any one tooth. Sometimes a burning or tingling occurred at the mucobuccal fold and this was sometimes accompanied by headache under the eyes, numbness, and pain in the maxilla or sinusitis. Negative X-ray findings, slight sensitivity to percussion, and conspicuous absence of fillings lead the authors to believe that maxillary pain during changes in atmospheric pressure is the result of aerosinusitis. They recommend that zinc oxide and eugenol be used as a base material for cavity preparations when dental pain is the result of pulpitis.

Dental services aboard a submarine are rendered by the pharmacist's mate only during dental emergencies. Routine care is given aboard the submarine tender for the personnel of submarines tied up alongside, and secondarily for relief crews and personnel of the tender. It is imperative that oral tissues of submariners be placed in good condition prior to extensive patrol periods in war areas. Toothache or tissue infection render a man impotent as a fighter at a time when his efficiency is a vital factor in the success of a submarine attack.

Aboard the submarine, dental caries is rampant and can be attributed to poor oral hygiene and a diet very high in carbohydrates. Martin (*2998*) 1946 reminds the reader that submariners are heavy coffee drinkers, drinking it "black and sweet." Cakes and pies are usually in evidence in the galley. There is lots of bread and jam, lots of potatoes and gravy—carbohydrate galore! A continued carbohydrate diet of this type increases susceptibility to dental caries.

Men with apparently sound teeth may, after several patrols, show evidence of caries activity. Such activity is difficult to detect by the regular mouth mirror and explorer examination. By the use of bite-wing X-rays these areas of caries activity may be demonstrated. As a general rule, all teeth with carious exposed pulps should be removed, and pulp cappings of exposed pulps are not recommended. In cases where the carious process has not progressed to such a degree, intermediate bases should be inserted in most cavities prior to placing the alloy filling material. This is particularly desirable in the 2 and 3 surface cavities.

Water distilled aboard the submarine is adequate for drinking and cooking purposes, but insufficient for frequent bathing. The shower room is secured most of the time unless a water reserve is built up. Dental hygiene is closely allied with bathing habits and many of the men admit that their toothbrushes remain unused day after day. Martin feels that the submariner just isn't "tooth-conscious" and considers brushing of the teeth too much trouble on a war patrol. A program of dental education for submarine personnel should be made a part of general hygiene and first-aid instruction, and could be accomplished by pamphlets, slide pictures, or lectures.

Disease of the gingival tissue may occur among personnel confined to a submarine for a long period of time. The etiology and treatment are adequately described in the dental literature elsewhere, and will not be included here because of lack of space. The factors listed for caries may contribute to the etiology of these conditions.

For other reports on dental problems, the reader may consult articles by Pigott (*3001*) 1944 and Schuessler (*3002*) 1947.

2996. Kennon, R. H. and C. M. Osborn. Relation of areodontalgia to aerosinusitis. *Air Surg. Bull.*, 1945, *2:* 434–435. [P]

2997. Kennon, R. H. and C. M. Osborn. Causes and treatment of aerodontalgia. *Air Surg. Bull.*, 1945, *2:* 442–443. [CH]

2998. Martin, W. B. Dental problems on submarines. *Nav. med. Bull., Wash.*, 1946, *46:* 898–900.

2999. Orban, B. Problems in aviation dentistry: Experimental studies of pulp changes produced in the decompression chamber. U. S. NRC–CAM. *OEMcmr–5779, C. A. M. Rept. no. 481,* 31 October 1945, 1 pp. [P]

3000. Orban, B., B. Ritchey, and H. A. Zander. Experimental study of pulp changes produced in the decompression chamber (1), (2). U. S. NRC–CAM. *Final rept., OEMcmr–559,* March 1946, 12 pp. [P]

3001. Pigott, J. P. Dental pain at high altitudes: origin and treatment. U. S. NRC–CAM. *C. A. M. Rept. no. 383, OEMcmr–38,* 23 October 1944, 8 pp.

3002. Schuessler, C. The effect of high altitude on oral tissues. *Milit. Surg.*, 1947, *100:* 318–322.

XIV. EFFECTS OF RADIOACTIVITY ON PERSONNEL

Modern warfare imposes additional dangers to the combatant man, and the advent of nuclear power and atomic bomb explosions has introduced radiation exposure as a real hazard. It is possible for a ship or submarine to be sound mechanically after an atomic explosion, yet radiological contamination

may make its operation temporarily dangerous to deck personnel. Underwater swimmers operating in radioactive waters are also subject to radiation from fission-product particles. The danger in handling or even approaching contaminated objects lies primarily in the harmful gamma radiation, although beta and alpha particles are an additional, if minor, hazard.

The literature included under this title is admittedly not complete. The papers selected have been chosen principally because they have been referred to in reports dealing with radiation sickness. For more complete descriptions of technical procedures and physiological effects of radiation, reference should be made to the classified literature. For general studies on radiation, papers by the following may be consulted: Behrens (*3005*) 1949 and (*3006*) 1951; Brues (*3010*) 1948; Cronkite and Chapman (*3014*) 1949; Dobson and Lawrence (*3016*) 1948; Dunham, Cronkite, Le Roy, and Warren (*3017*) 1951; Warren (*3033*) 1942; Warren and Bowers (*3037*) 1950; and Warren and Draeger (*3038*) 1946. An anonymous paper (*3040*) 1951 is also listed.

The clinical picture in radiation sickness has been described by Brues (*3011*) 1950. Following a single, brief exposure of the total body to a lethal dose of ionizing radiation, there is a latent period of one or more hours during which no manifestations are seen. This is followed by a period of prostration, which varies somewhat with the species. In dog and man, vomiting and listlessness are observed. Superficial hyperemia and evidence of transudation of plasma from the capillaries are noted during this period. There is some evidence that the initial response is mediated through the parasympathetic system, since it may be alleviated in part by atropine and vagotomy.

Subsequent to the initial reaction there is a loss of appetite accompanied by greatly decreased food and water intake, and examination of the blood shows a precipitous fall of total white-cell count and the various cell types, ordinarily preceded by an increase in granular leukocytes, as seen in acute pyogenic infections. During the acute phase, which usually appears during the second week, the white-cell count is greatly depressed. This is ordinarily accompanied by widespread gastrointestinal ulceration and gingivitis. The anemia seen in this stage is due to failure of red-cell formation and to destruction of red cells already present. Fever, tachycardia, increased rate of red-cell formation, and sedimentation rates are observed in the third and fourth weeks. The delayed blood clotting and spontaneous bleeding into various sites have been shown to be the result of an increased concentration of heparin in the blood and can be counteracted by judicious use of protamine or toluidine blue, which combine with heparin.

In addition, there is impairment of intestinal glucose absorption and a shift in the salt and water balance. Sublethal doses result in sterility in the male but, as a general rule, survivors recover the ability to form sperm within a few months. Terminally, the state resembles irreversible shock following massive trauma or hemorrhage or the terminal stages of overwhelming infectious disease. The blood pressure is depressed and renal function approaches zero.

For other reports on clinical symptoms of radiation sickness, papers by the following may be consulted: Cronkite (*3012*) 1949; Hempelman, Lisco, and Hoffman (*3021*) 1952; Le Roy (*3025*) 1947; Nims (*3026*) 1949; Prosser (*3028*) 1947; and Raper (*3029*) 1950.

The bleeding tendency, attributed to an increase of circulating heparin, was investigated by Allen and Jacobson (*3003*) 1947. Both bleeding and clotting times are prolonged, and this is accompanied by a thrombocytopenia. At death, hemorrhage is first seen in organs of motion such as the heart, intestines, lungs, urinary bladder, and skeletal muscle. The clotting time is returned to normal by antiheparin substances, and therefore thrombocytopenia does not, per se, appear to play an important role in hemorrhage. The administration of vitamins K and C, calcium salts, and fresh, whole blood did not prevent hemorrhage.

Experimental work by Cronkite (*3013*) 1950 and Cronkite, Ulrich, Eltzholtz, Sipe, and Schork (*3015*) 1949 on the hemorrhagic syndrome of acute ionizing radiation indicates that this phenomenon is the result of increased vascular fragility and thrombocytopenia. Evidence was presented suggesting that serum fibrinolysis may have been activated also.

Observations on the radiation effect of atomic bombing are reported by Beck and Meissner (*3004*) 1946. Bone-marrow studies on 20 Nagasaki patients demonstrated an anemia, neutropenia, and thrombycytopenia. Seven post-morten examinations confirmed this bone-marrow damage. Recovery of the bone marrow was noted clinically. Lawrence (*3023*) 1949 investigated the urinary excretion pattern of 17-ketosteroids in 11 dogs following exposure to a minimal lethal dose of total body X-radiation. All animals exhibited a significant increase in steroid excretion at some time between the 5th and 12th day following radiation. These values then fell to normal or subnormal levels by the 30th to 40th day.

This excretion pattern is interpreted to indicate an alteration of adrenal cortical and/or testicular activity.

The cellular effects of radiation are reported in papers by Failla (*3019*) 1940, Lea (*3024*) 1946, and Warren (*3032*) 1942 and (*3035*) 1944. The review by Warren (*3035*) gives the following most recognizable cell changes after radiation exposure: (1) inhibition of mitosis; (2) breakage of chromosomes; (3) lagging of chromosomes; (4) complete or partial adhesion of chromosome pairs; and (5) asymetry of mitosis. Vacuolation of the cytoplasm is the most consistent feature. Lea (*3024*) 1946 believes that decomposition of proteins and other cell constituents by radiation may be injurious even in low concentrations, and recommends investigation of this matter. The overall chemical change may be small, but locally it may be high.

For general studies on radiation pathology, papers by the following may be consulted: Benkwith (*3007*) 1946; Bloom (*3008*) 1948; Brown, Hardenbergh, and Tullis (*3009*) 1951; Schlaegel (*3030*) 1947; Tullis and Warren (*3031*) 1947; Warren (*3034*) 1942 and (*3036*) 1946; and Zirkle (*3039*) 1951. The study by Bloom is a large, definitive volume on the histopathology of irradiation published as one of the health volumes in Division IV of the National Nuclear Energy Series. Zirkle has reported gross effects of beta irradiation on restricted surfaces of rabbits following varying doses of radiation. The main effects in order of appearance were (1) erythema; (2) pigmentation; (3) epilation; (3) loss of outer layer of skin; (5) crust formation; (6) healing; and (7) regrowth of hair. Damage to the skin produced by massive doses of beta rays resembled thermal burns but showed two important differences. The various stages of beta damage required 4 to 7 times as long to develop, and secondly, the indirect action was confined to superficial tissue. Gross effects to total-surface beta irradiation includes (1) inflammation of the eyelids; (2) erythema in the ears and feet; (3) closure of the eyes; (4) epilation and desquamation around the eyes, mouth, and nostrils; (5) ulceration; (6) regrowth of hair; and (7) tumor formation.

3003. Allen, J. G. and L. O. Jacobson. Hyperheparinemia: cause of the hemorrhagic syndrome associated with total body exposure to ionizing radiation. *Science*, 1947, *105:* 388–389. [R]

3004. Beck, J. S. P. and W. A. Meissner. Radiation effects of the atomic bomb among the natives of Nagasaki, Kyushu. *Amer. J. clin. Path.*, 1946, *16:* 634–639.

3005. Behrens, C. F. *Atomic medicine.* New York, Thomas Nelson & Sons, 1949, 416 pp.

3006. Behrens, C. F. Permissible dosage and considerations of calculated risk. U. S. Navy. NMRI. *Lecture and review series no. 51–7,* 2 July 1951, 21 pp.

3007. Benkwith, K. B. Retinal hemorrhage as seen in an atomic-bomb casualty. *Amer. J. Ophthal.*, 1946, *29:* 799–800. [CH]

3008. Bloom, W. *Histopathology of irradiation from external and internal sources.* New York, McGraw-Hill Book Co., Inc., 1948, xxv, 808 pp.

3009. Brown, C. S., E. Hardenbergh, and J. L. Tullis. The biochemical, cellular, and bacteriologic changes in thoracic duct lymph of dogs exposed to total body irradiation. U. S. Navy. NMRI. *Project NM 006 012.04.29,* 14 pp.

3010. Brues, A. M. Pathologic effects of ionizing radiations and radioactive materials. *Proc. Soc. exp. Biol., N. Y.*, 1948, *42:* xxii.

3011. Brues, A. M. Radiation sickness. pp. 778–781 in: *Medical physics. Volume II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

3012. Cronkite, E. P. The clinical manifestations of acute radiation illness in goats. *Nav. med. Bull., Wash.*, 1949, *49:* 199–215.

3013. Cronkite, E. P. The hemorrhagic syndrome of acute ionizing radiation illness produced in goats and swine by exposure to the atomic bomb at Bikini, 1946. U. S. Navy. NMRI. *Project NM 006 012.04.33,* 21 December 1950, 45 pp. *Blood,* 1950, *5:* 32–45. [P]

3014. Cronkite, E. P. and W. H. Chapman. A critical analysis of the syndrome of acute total body radiation illness, its role in atomic warfare and its influence on the future practice of military medicine. U. S. Navy. NMRI. *Project NM 007 039, Rept. no. 13,* 3 January 1949, 23 pp. *Milit. Surg.*, 1949, *104:* 7–21.

3015. Cronkite, E. P., F. W. Ullrich, D. C. Eltzholtz, C. R. Sipe, and P. K. Schork. The response of the peripheral blood of swine to whole body X-ray radiation in the lethal range. U. S. Navy. NMRI. *Project NM 007 039. Rept. no. 21,* 7 April 1949, 11 pp.

3016. Dobson, R. L. and J. H. Lawrence. Physiological effects of radiant energy. *Annu. Rev. Physiol.*, 1948, *10:* 479–500. [R]

3017. Dunham, C. L., E. P. Cronkite, G. V. Le Roy, S. Warren. The syndrome of acute radiation injury due to exposure of the whole body to the initial nuclear radiation of an atomic bomb. U. S. Navy. NMRI. *Lecture and review series no. 51–10,* 7 August 1951, 11 pp.

3018. Ellinger, F. Newer concepts of radiation sickness and its treatment. U. S. Navy. NMRI. *Lecture and review series no. 51–6,* 23 May 1951, 14 pp.

3019. Failla, G. Some aspects of the biological action of ionizing radiations. *Amer. J. Roentgenol.*, 1940, *44:* 649–664.

3020. Fulton, J. D., A. C. Arnold, R. B. Mitchell, and M. B. Danford. The antibody response of animals exposed to X-radiation. III. The protective effect of chemotherapeutic agents of a specific immune status of X-radiated mice. USAF. Randolph Field, Tex. School of aviation medicine. *Project 21–47–002, Rept. no. 3,* October 1951, iii, 15 pp.

3021. Hempelmann, L. H., H. Lisco, and J. G. Hoffman. The acute radiation syndrome: A study of nine cases and a review of the problem. *Ann. Intern. Med.*, 1952, *36:* 279–510. [CH]

3022. Kaplan, S. J., C. D. Tait, Jr., P. D. Wall, and R. B. Payne. Behavioral changes following radiation. I. Study of retention of a partially learned maze habit. USAF. Randolph Field, Tex. School of aviation medicine. (Unnumbered project), Rept. no. 1, March 1951, 33 pp.

3023. Lawrence, G. H. The effect of total body X-radiation on 17-ketosteroid excretion in dogs. U. S. Navy. NMRI. *Project NM 007 039, Rept. no. 22,* 14 June 1949, 12 pp. [P]

3024. Lea, D. E. *Actions of radiations on living cells.* Cambridge, University Press. 1946, xii, 402 pp.

3025. LeRoy, G. V. The medical sequelae of the atomic bomb explosion. *J. Amer. med. Ass.,* 1947, *134:* 1143–1148.

3026. Nims, L. F. Radiation. *Annu. Rev. Physiol.,* 1949, *11:* 527–544. [R]

3027. Pickering, J. E. Evaluation of the Land Self-Developing Film Badge dosimeter. USAF. Randolph Field, Tex. School of aviation medicine. *Special rept.,* May 1951, 4 pp.

3028. Prosser, C. L. The clinical sequence of physiological effects of ionizing radiation in animals. *Radiology,* 1947, *49:* 299–313. (Spanish summary.)

3029. Raper, J. R. Beta rays: biologic effects. pp. 66–71 in: *Medical physics. Volume II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

3030. Schlaegel, T. F., Jr. Ocular histopathology of some Nagasaki atomic-bomb casualties. *Amer. J. Ophthal.,* 1947, *30:* 127–135.

3031. Tullis, J. L. and S. Warren. Gross autopsy observations in the animals exposed at Bikini. *J. Amer. med. Ass.,* 1947, *134:* 1155–1158.

3032. Warren, S. Effects of radiation on normal tissues. *Arch. Path.*, Chicago, 1942, *34:* 443–450. [R]

3033. Warren, S. Effects of radiation on normal tissues. Dunlap, C. E. III. Effects of radiation on the blood and the hemopoietic tissues, including the spleen, the thymus and the lymph nodes. *Arch. Path., Chicago,* 1942, *34:* 562–608. [R]

3034. Warren, S. Effects of radiation on normal tissues. V. Effects on the respiratory system. *Arch. Path., Chicago,* 1942, *34:* 917–931. [R]

3035. Warren, S. The histopathology of radiation lesions. *Physiol. Rev.,* 1944, *24:* 225–238.

3036. Warren, S. The pathologic effects of an instantaneous dose of radiation. *Cancer Res.,* 1946, *6:* 449–453. [D]

3037. Warren, S. and J. Z. Bowers. The acute radiation syndrome in man. *Ann. intern. Med.,* 1950, *32:* 207–216.

3038. Warren, S. and R. H. Draeger. The pattern of injuries produced by the atomic bombs at Hiroshima and Nagasaki. *Nav. med. Bull., Wash.,* 1946, *46:* 1349–1353.

3039. Zirkle, R. E. *Effects of external beta radiation.* First edition. New York, McGraw-Hill Book Co., Inc., 1951, 242 pp.

3040. Anon. Atomic-powered submarine. *Mech. Engr.,* 1951, *73:* 17.

Protection and Preservation of Personnel

I. GENERAL STUDIES

It is not sufficient to select personnel with high physiological and psychological reserves and with high tolerance of stress. Superimposed upon a realistic and efficient selection program must be efforts to protect personnel from intolerable stresses by attention to habitability, food and water supply, clothing, and special equipment and devices. In all procedures and plans for protection and preservation of personnel, it must be borne in mind that the submarine is a fighting vessel. The effective fighting power of the submarine is the primary consideration, and all matters of protection and comfort of personnel are important in the degree to which they contribute to this.

3041. Gt. Brit. Ministry of labour and national service. Part VI. Diving operations. pp. 29–30 in: *Factories acts, 1937 and 1948, Work of engineering construction.* London, His Majesty's Stationary office, 1951, 55 pp.

3042. Kopecky, E. F., L. M. Biggs, and H. A. Lindsey. Comparison of the semirigid stretcher (NMRI Model A) now carried by most submarines with the Peters emergency stretcher. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 011 019, Rept. no. 1,* 31 March 1948, 5 pp.

3043. Pointner, R. Clinical investigations with submariners. pp. D:I-1—D:I-22 in: *Monograph on submarine medicine. Folio VII,* Germany. U. S. Zone. Office of naval advisor. 1948. [P]

3044. Southwell-Sander, G. H. G. Recent advances in naval hygiene and preventive medicine. *J. R. nav. med. Serv.,* 1947, *33:* 294–305. [R]

3045. U. S. Navy. BuMed. Submarine medicine. pp. 198–212 in: *A manual of naval hygiene.* Government Printing Office, Washington: 1943, 340 pp.

II. HABITABILITY

A. LIGHTING

The subject of artificial illumination is of basic importance in all inside working and living environments, including the submarine. To maintain healthful and efficient visual function, it is necessary to provide adequate lighting. In the submarine only artificial illumination is used, and a unique situation is provided by this environment for the study of basic lighting requirements and the application of new lighting technique. The overheads tend to be low, and much of the overhead and wall space is occupied by pipes, conduits, dials, and other machinery. The deck space is confined largely to narrow passageways and walks. It is evident therefore that special lighting problems are presented, and that in most cases illumination layouts of home and office cannot be transferred without modification to the submarine situation.

A report by Tinker (*3062*) 1949 surveys the lighting and painting conditions in several submarines. The most common deficiencies were found to be: (1) insufficient light at the places where visual discriminations have to be made; (2) marked brightness contrasts in adjoining surfaces; (3) lack of adequate uniformity in distribution of illumination; (4) disturbing spectral reflections from shiny surfaces such as highly polished valve and switch handles; and (5) glare from excessively bright and poorly located light sources. The author reviews the spectral quality of color of light as it applies to submarine problems. He states that for threshold seeing, spectral yellow, or yellow light from sodium vapor lamps, is slightly more effective than other artificial illuminations. No illuminant is better than diffused daylight.

Intensity of illumination was considered in relation to visual acuity, size of object to be discriminated, speed of vision, brightness contrast, and efficiency of performance. There are indications that visual efficiency of normal eyes increases rapidly as illumination is increased from a fraction of 1 up to 5 foot-candles, more slowly from there up to about 10 foot-candles, and very slowly from 10 to about 20 foot-candles. When the object is small, visual efficiency improves by practical amounts up to 40 or 50 foot-candles.

Visual efficiency and visual comfort are reduced by two factors of distribution: (1) glare from bright spots in the field of vision, and (2) marked brightness contrast between areas in the field of vision. Tinker (*3063*) 1950 recommends that illumination be as uniform as possible, and that brightness contrasts between adjoining areas be small. Painted bulkheads, overheads, and furnishings should be pleasing and should provide reflecting surfaces.

The paint should be light enough to reflect a large portion of incident light: overheads, 70 to 80 percent; bulkheads, 40 to 50 percent; desk tops, 30 to 40 percent; and floors, 20 to 25 percent. Good decorative schemes can be executed with a low brightness contrast of around 3 to 1.

Interior decoration of the U. S. S. *Cutlass* in 1949 is described by Dewey (*3051*) 1950. "Operation Rainbow" was initiated at the Philadelphia Navy Yard to increase the habitability of the submarine by the medium of color and lighting. Three different colors were used, making each compartment different from its neighbor. The color shades were green-gray, yellow-gray, and medium gray. Ladders and apparatus were painted also to give a feeling of expansiveness. Strong colors were not used because it was felt that such visual stimulation caused fatigue. Individual bedlamps were used to increase the opportunity for sleep of crew members in the same compartment. Continuously lighted compartments were illuminated by indirect lighting to add to the feeling of depth and expansiveness, and the decks were tiled in brown to give an "earthy" atmosphere.

The general subject of illumination is discussed by Farnsworth (*3052* and *3053*) 1950 with emphasis on intensity of illumination and spectral quality of light as they apply to the job performed. Insufficient illumination may cause fatigue and inefficiency, and continued effort under these conditions may result in eyestrain, astigmatism, myopia, and headaches. Differences in work efficiency while exposed to white and monochromatic light are insignificant. The author states that a room may be correctly lighted from a visual hygiene and working efficiency standpoint, but still may cause an unpleasant feeling. A flatly lighted area is less pleasant than one with gradations. The light should diffuse over the room or compartment and blend into other lights with a moderate amount of contrast. The Tufts College report (*3064*) 1949 states that an objection against modern lighting arises from the uncomfortable effects of high brightness. When the general brightness level is low, then relatively high brightness ratios become acceptable, and when the adaptive level is raised, then the brightness ratio must be reduced to remain acceptable.

For a review of illumination problems as related to the working environment, the reader should consult reports by Brandt (*3048*) 1947; Chapanis, Garner, and Morgan (*3049*) 1949; Crouch (*3050*) 1945; and Hoffman (*3057*) 1947. A report by Schaefer (*3060*) in 1948 indicated that the researcher, when studying the effects of illumination, must also consider the photodynamic effect; i. e., optical sensitization by which the fluorescing substances of the organism are rendered sensitive to rays of light which normally are inactive. These substances are adrenalin, biliary pigments, vitamin D, and the carotinoids. He states that the withholding of chemotonic and sensutonic effects of light from the organism could cause a persistent condition of vagotonia. Stimulation of the vegetative system is reduced in montonous and gloomy environments.

Lack of sunlight experienced by submarine personnel during World War II was a cause for some concern, and the possibility of longer periods away from sunlight presented by snorkel operation may heighten interest in this field again. During World War II, ultraviolet lamps were used in a few submarines for sunbathing by the crew and disinfection of the air by installing these lamps in the air ducts. A report by Blum (*3046*) in 1944 indicated that few if any beneficial effects were derived from irradiation by mercury arc lamps. There was a value associated with morale. Reports by Boeder (*3047*) 1950 and Ludwigh and Kinsey (*3059*) 1946 state that ultraviolet radiations longer than 365 millimicrons are without deleterious effect on the functions of the normal eye.

For other general reports on illumination, the reader may consult articles by Grether (*3054*) 1948; Hall and Greenbaum (*3055*) 1950; Hanes (*3056*) 1950; Kuhn (*3058*) 1950; Tinker (*3061*) 1946; U. S. Navy (*3065*) 1943; and Witheridge (*3066*) 1948.

3046. Blum, H. F. The advisability of mercury arc lamps for irradiation of personnel of submarines. U. S. Navy. NMRI. *NH6–1/All/NMRI–47,* 25 February 1944, pp. 5.

3047. Boeder, P. The effect of ultraviolet on the human eye. *Amer. J. Optom.,* 1950, *27:* 437–447.

3048. Brandt, A. D. Industrial illumination. pp. 298–321 in: *Industrial health engineering.* New York, John Wiley & Sons, Inc., 1947, 395 pp. [D]

3049. Chapanis, A., W. R. Garner, and C. T. Morgan. The working environment. Light and color. pp. 417–419 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

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3052. Farnsworth, D. Illumination. pp. 60–68 in: *Handbook of applied psychology. Volume I.* Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart & Co., Inc., 1950, ix, 380 pp. [R]

3053. Farnsworth, D. Illumination. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 003 041.18, Rept. no. 5,* 1950, 9 pp.

3054. Grether, W. F. Dial reading performance as related to illumination variables. II. Spectral distribution. USAF. Wright-Patterson air force base, Dayton, Ohio.

Aero medical laboratory. *Tech. rept. no. MCREXD–694–21A,* 1 December 1948, 26 pp. [P]

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3056. Hanes, R. M. Some effects of shape on apparent brightness. *J. exp. Psychol.,* 1950, *40:* 650–654.

3057. Hoffman, A. C. Luckiesh and Moss on reading illumination. *J. appl. Psychol.,* 1947, *31:* 44–53.

3058. Kuhn, H. S. Illumination. pp. 287–306 in: *Eyes and industry.* Second edition. St. Louis, C. V. Mosby Co., 1950, 378 pp.

3059. Ludvigh, E. and V. E. Kinsey. Effect of long ultraviolet radiation on the human eye. *Science,* 1946, *104:* 246–247. [P]

3060. Schaefer, K. E. Deficiency of light. pp. B: I–30—B: I–32 in: *Monograph on submarine medicine, Folio I.* Germany. U. S. Zone. Office of naval adviser. 1948.

3061. Tinker, M. A. Illumination standards. *Amer. J. publ. Hlth.,* 1946, *36:* 963–973.

3062. Tinker, M. A. Lighting and color. pp. 357–374 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3063. Tinker, M. A. Building illumination. pp. 283–288 in: *Handbook of applied psychology. Volume I.* Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart & Co., Inc., 1950, ix, 380 pp.

3064. Tufts College. Illumination. 12 pp. in: *Handbook of human engineering data for design engineers.* Tufts College, Institute for applied experimental psychology. *SDC Human Engineering Project 20–G–1, Project Designation NR–783–001, Technical Report 199–1–1,* 1 December 1949, 410 pp.

3065. U. S. Navy. BuMed. Lighting of ships. pp. 55–64 in: *A manual of naval hygiene.* Government Printing Office, Washington, D. C., 1943, 340 pp.

3066. Witheridge, W. N. Light condition. pp. 119–127 in: *Industrial hygiene and toxicology.* New York, Interscience Publishers, Inc., 1948, 531 pp.

B. VENTILATION AND AIR CONDITIONING

1. GENERAL STUDIES

Existence on a submarine is characterized by very crowded living and sleeping conditions, limited water supply, frequent high temperatures and humidity resulting from engineroom heat and shutting down of ventilation during certain periods of enemy contact and, finally, toxic levels of carbon dioxide and decreased concentrations of oxygen. A number of reports dealing with general problems of ventilation and air purification have been selected from the large volume of literature on air conditioning as being of possible application to the problems as encountered in the submarine service. References of a general nature have been listed below.

3067. Bedford, T. The quality of the air. pp. 129–152 in: *Basic principles of ventilation and heating.* London, H. K. Lewis & Co., Ltd., 1948, 401 pp.

3068. Behnke, A. R., F. C. Houghten, W. V. Consolazio, and N. Pace. Physiologic principles underlying naval ventilation. U. S. Navy. Naval medical school, Department of atmospheric hygiene, Bethesda, Md. November 1942, 69 pp.

3069. Bennet, M. G. Notes on visit to H. M. Submarine *Tradewind.* Gt. Brit. MRC–RNPRC, CES. *R. N. P. 49/520, C. E. S. 284,* 26 January 1949, 2 pp.

3070. Brandt, A. D. Heating, ventilating, and air conditioning for temperature, humidity, comfort, and odor content. pp. 280–290 in: *Industrial health engineering.* New York, John Wiley & Sons, Inc., 1947, 395 pp. [D]

3071. Chapanis, A., W. R. Garner, and C. T. Morgan. The working environment. Atmospheric effects. pp. 396–408 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc., 1949, 421 pp.

3072. Dewey, H. S. Submariner explains importance of undersea air conditioning. *Heat Pip. Air Condit.,* 1950, *22:* 102–103.

3073. Du Bois, E. F. Methods of air purification. pp. 23–31 in: *Review of recent work on air purification in submarines.* U. S. Navy. BuMed. Submarine ventilation. *Bulletin no. 4 (126632),* March 15, 1919, 47 pp.

3074. Gt. Brit. MRC–RNPRC, CES. Memorandum on air hygiene in warships. *R. N. P. 48/446, C. E. S. 243,* April 1948, 3 pp.

3075. Herrington, L. P. Industrial ventilation. pp. 288–297 in: *Handbook of applied psychology. Volume I.* Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart & Co., Inc., 1950, ix, 380 pp.

2. AIR FLOW AND VOLUME

Air-conditioning requirements vary according to the special conditions of the installation, which may be in a theater, factory, store, submarine, or any other enclosure occupied by human beings. Modern engineering practice of air conditioning involves two phases: (1) actual conditioning of air, that is, the controlled alteration of its temperature, humidity, purity, carbon dioxide level, and oxygen concentration; and (2) ventilation, or replacement of stale air in an enclosure by conditioned air. Correct air conditions are essential for proper functioning of mechanical equipment. Apart from the mechanical reaction, considerations of health, efficiency, and morale of the human occupants require that the air be fit to breathe. This requires the removal of fumes from a ship's galley, engineroom, battery room, and waterclosets. Stale air must be replaced by fresh air. Moreover, the body gives off excess heat and moisture in the expired air and the air in contact with the surface of the body.

Of interest experimentally were the responses of men exposed to wind velocities ranging between 10 and 100 feet per minute and wet-bulb temperatures above 80° F. The subjects were observed over 4-hour periods during which they either sat still or worked. Dunham, Holling, Ladell, McArdle, Scott, Thomson, and Weiner (*3091*) 1946 found that environments with the air moving at speeds between 10 and 75 feet per minute were extremely uncomfortable when the men were working in overalls

at high dry- and wet-bulb temperatures. An increase in the velocity of air movement above 75 feet per minute partially alleviated this condition, but speeds above 300 feet per minute gave no significant increases in comfort. When the temperature of the air was above 100° F., conditions were made more intolerable by raising the rate of air movement above 300 feet per minute. Ventilation conditions in the submarine are reported by Schaefer (*3096*) 1948. In this report on the problems of ventilation encountered on German submarines during World War II, the author describes the uncomfortable effects of high-velocity air movement channeled to men from small air ducts. In a report by Ellis (*3092*) 1948, the author states that submarine crews in northern waters are subjected to cold air drawn aft from the conning tower to the engineroom, but while in tropical waters this movement of warm air reduces the efficiency of the air-conditioning plant. It was found that the volume of breathable air available for each man in the submerged submarine is somewhere between 300 and 500 cu. ft.

In an investigation of the minimal quantity of replenishment air required in a living space to keep odors at an acceptable level in conjunction with the use of air cooling and activated carbon, Consolazio and Pecora (*3090*) 1946 found that, with air cooling alone, 5 cu. ft. per minute per man (3 cu. ft. per minute per bunk) of replenishment air would keep the odors at acceptable levels. The odor level in an air-cooled space was found to be dependent upon the following factors: (1) quantity of replenishment air; (2) temperature and humidity of the compartment air; (3) quantity of water condensed in the cooling coils; (4) hygiene of the occupants and cleanliness of the space; and (5) activity of the occupants. With activated carbon the replenishment air could be further reduced to values as low as 1 cubic foot per minute per man.

For additional reports on volume and air flow, the reader should consult reports by Gt. Brit. MRC–RNPRC (*3093*) 1950; Nelson, Eichna, Shelley, and Horvath (*3094*) 1946; and Nothdurft (*3095*) 1946.

3076. Chuiton, [ ]le. Les problèmes d'hygiène que pose la vie a bord des sous-marins. *Sem. Hop. Paris,* 1948, *24:* 198–201.

3077. Leopold, C. S. Conditions for comfort. *Trans. Amer. Soc. Heat. and Vent. Engrs.,* 1947, *53:* 295–304. [R]

3078. Nothdurft, H. The necessity of air conditioning in combat submarines in the German navy. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 46/286; H. S. 131,* undated, 5 pp.

3079. Scott, J. W. Conditions in H. M. S. *Devonshire* en route from Devonport, England, to Sydney, Australia, in September and October 1945. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 45/259, H. S. 102,* December 1945, 6 pp.

3080. Scott, J. W. and D. Y. Solandt. Survey of lighting and ventilation in barracks and in ships of the Royal Canadian Navy. Canada NRC. Proceedings of second meeting of associate committee on naval medical research. *Project C4050,* 7 October 1943, 2 pp.

3081. Sellers, E. A. and J. M. Parker. Outline of proposed trials of air conditioning in frigates. Canada NRC. Proceedings of the fourth meeting of associate committee on naval medical research. *Project C4118,* 16 February 1945, 7 pp.

3082. Smith, K. R. Ventilation. pp. 68–74 in: *Handbook of applied psychology. Volume I.* Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart & Co., Inc., 1950, ix, 380 pp.

3083. Stiening, F. H. Air conditioning. Factors affecting human comfort and health: Fundamental requirements of an air conditioning system. pp. 202–209 in: *Introduction to industrial medicine.* Edited by T. Lyle Hazlett. Second edition. Chicago, Industrial Medicine Publishing Co., 1947, 260 pp.

3084. Urdahl, T. H. and W. C. Whittlesey. Warship ventilating, heating and air conditioning. *Trans. Amer. Soc. Heat. and Vent. Engrs.,* 1943, *49:* 35–48. Discussion by J. W. Markert. [R]

3085. U. S. Navy. BuMed. Ventilation of submarines. pp. 31–36 in: *A manual of naval hygiene.* United States Government Printing Office, Washington, D. C., 1943, 340 pp.

3086. U. S. Navy. BuNavPers. Habitability and submarine health. pp. 156–174 in: *Submarine medicine practice. NavPers 10838,* March 1949, 182 pp. [D]

3087. Winslow, C. E. A. and L. P. Herrington. The objectives of air conditioning. pp. 163–197 in: *Temperature and human life.* Princeton, Princeton University Press, 1949, 272 pp.

3088. Witheridge, W. N. Air conditioning. pp. 107–119 in: *Industrial hygiene and toxicology.* Edited by Frank A. Patty. New York, Interscience Publishers, Inc., 1948, 531 pp.

3089. Witheridge, W. N. Ventilation. pp. 275–348 in: *Industrial Hygiene and Toxicology. Volume I.* Edited by F. A. Patty. New York, Interscience Publishers, Inc., 1948, ix, 531 pp. [R]

3. HUMIDITY CONTROL

There is in the submarine a continuous evaporation of moisture into the air from four main sources: (1) storage batteries, (2) cooking, (3) human occupants, and (4) bilges. Space can be made available for sufficient air-conditioning machinery to control the dewpoint. Control of the dewpoint means control of the relative humidity, and it is the relative humidity more than the mere temperature of the air that causes discomfort. With a build-up of a thousand pounds of moisture per day in the air of a submarine, relative humidity becomes a factor of major significance.

Humidity control in submarines is important, but it is just as important a problem in industry. Because of the engineering ramifications it is not intended under this heading to discuss the extensive

literature on methods of regulating humidity. For a report on humidity problems aboard the submarine, a paper by Schaefer (*3097*) 1948 should be consulted. The relative humidity levels usually range between 70 and 90 percent in submarines operating in the middle latitudes. Lower relative humidities are present in the enginerooms where the temperatures are higher, but when calculated as vapor pressure, they are equivalent to the rest of the boat. Under long periods of submergence, moisture is dammed up in the submarine at an air temperature of 20° C.

3090. Consolazio, W. V. and L. J. Pecora. Minimal replenishment air required for living spaces under conditions of mechanical cooling and in conjunction with the removal of odors by activated carbon and other means. U. S. Navy. NMRI. *Project X–533, Rept. no. 4,* 26 July 1946, 23 pp. [P]

3091. Dunham, W., H. E. Holling, W. S. S. Ladell, B. McArdle, J. W. Scott, M. L. Thomson, and J. S. Weiner. The effects of air movements in severe heat. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 46/316, H. S. 152,* August 1946, 20 pp. [P]

3092. Ellis, F. P. Environmental factors affecting health and efficiency in warships. *Publ. Hlth., Lond.,* 1948, *61:* 104–107. *Brit. med. J.,* 1948, *1:* 587–592. *J. industr. Hyg.,* 1948, *30:* abstract section: 86. [R]

3093. Gt. Brit. MRC–RNPRC, CES. Recirculation of air in warships. *R. N. P. 50/635, C. E. S. 333,* 15 November 1950, 3 pp.

3094. Nelson, N., L. W. Eichna, W. B. Shelley, and S. M. Horvath. The effect of air movement on the loss of heat by evaporation, convection, and radiation from nude and clothed individuals. *Fed. Proc. Amer. Soc. exp. Biol.,* 1946, *5:* 76.

3095. Nothdurft, H. The necessity of air conditioning in combat submarines in the German navy. Gt. Brit. MRC–RNPRC, HS. *R. N. P. 46/286, H. S. 131,* 18 December 1946, 5 pp.

3096. Schaefer, K. E. Conditions of ventilation on board. pp. B: I–16—B: I–28 in: *Monograph on submarine medicine, Folio I,* Germany. U. S. Zone. Office of naval advisor. 1948.

3097. Schaefer, K. E. The humidity aboard the submarine. pp. B: I–14—B: I–16 in: *Monograph on submarine medicine, Folio I,* Germany. U. S. Zone. Office of naval advisor. 1948.

4. TEMPERATURE CONTROL

When the ocean or tropical air is warmer than the submarine, there is a passage of heat from the water into the boat. Heat is also added internally by hot engines, storage batteries, galley stove, electric lights, radio and radar equipment, and the human occupants. An adult, when engaged in light work, gives off approximately 500 B. t. u. per hour. In comparison, a 25-watt electric light bulb gives off 85 B. t. u. per hour. Therefore, in a small enclosure as in the submarine, the rise in temperature and moisture of the air caused by the presence of a number of people is considerable.

Information concerning the indices of comfort in moving air may be obtained from papers by Yaglou (*3108* and *3110*) 1947 and 1949. According to the author, the effective temperature scale overestimates greatly the influence of humidity at the lower temperatures, and not enough allowance is made for humidity at the higher temperatures which approach the limit of man's endurance to heat. This disability is attributed to absorption and adaptation phenomena, which had been overlooked in the index. A rational method is proposed for correcting the index on the basis of mean skin temperature. Kellogg (*3104*) published a paper in 1946 on the critical factors in minimal air cooling of living quarters. Studies were made on a group of 12 men, previously acclimatized to severe heat and maintained continuously for periods of 4½ days at each of a series of humidities in the dry-bulb temperature range from 76° to 93° F. (73° and 83° E. T.). The skin temperature rose to 94° and 95° F. at a dry-bulb temperature of 81° to 83° F., and remained in this range at the higher dry-bulb temperatures. Evaporative water loss during light activity varied with dry-bulb rather than with effective temperature, and was doubled with increases in dry-bulb temperatures between 79° and 86° F. The subjective response to temperature and skin wetness varied with the effective temperature rather than the dry-bulb temperature. The "just right" temperature arrived at by interpolation was found to be about 76° E. T. Practically all skins appeared to be "dry" at temperatures below 76° E. T. For the regimen employed, the threshold for producing heat rash seemed to lie between 82° and 84° F. with high humidities, and between 87° and 89° F. at low humidities. The men slept comfortably and did not develop heat rash when the effective temperature did not exceed 78° and the dry-bulb temperatures did not extend beyond 85° F.

For a discussion of factors contributing to pleasant environments as related to temperature, the reader should consult a monograph by Bedford (*3100* and *3101*) 1948. The author found that with the cool-air, warm-wall environment the mean skin temperature is lower than when the air and walls were at the same temperature. A sudden drop of temperature (10° F.) is harmful to man in the tropics when the skin and clothing are wet with perspiration. The initial chilling suppresses sweating and may reduce man's ability to withstand heat for some time after returning to the hot atmosphere. Maximum comfort was attained when the skin temperature on the head, sternum, cheek, and the area over the carotid artery was 92.3° F. Man feels

"too cool" when the temperature of the skin over these areas is below 89° F., and temperatures above 96° F. give the sensation of being "too warm." A report by the Climatic Efficiency Subcommittee of the Great Britain Medical Research Council (*3103*) 1951 stated that the 80° F. effective temperature should represent the upper desirable limit for environmental standards with 86° F. effective temperature as the upper tolerable limit.

The American Society of Heating and Ventilating Engineers (*3098*) 1951 presents evidence that in machinery spaces it is more practicable to use spot cooling of personnel at working areas than to attempt to obtain uniform ambient temperature. They also state that the minimum quantity of ventilation air required for sleeping spaces should be that which will limit the temperature rise over that of the outside air to not more than 10° F., or a minimum of 30 cu. ft. per minute per person, whichever is greater. The optimum temperature for berthing spaces is stated to be 70° F. Galley and food-handling spaces should have the air changed once every 1 to 4 minutes.

The use of electrically heated foot-warming panels as a means of alleviating foot discomfort in naval personnel on duty in cold bridge areas of ships was investigated by Yaglou (*3111*) 1950. The efficient use of the heating panel was found to be limited to conditions of low wind velocities and temperatures above 0° F. In the presence of appreciable winds the panel's effectiveness is greatly reduced and the power consumption becomes too great in comparison with that of other methods of keeping the feet, or the whole body, warm. Additional data on this subject are supplied in the papers by Nielsen (*3105* and *3106*) 1948.

It is suggested that readers wishing to obtain further information on temperature control consult papers by the American Society of Heating and Ventilating Engineers (*3099*) 1951; Crowden and Angus (*3102*) 1947; Reese (*3107*) 1947; and Yaglou (*3109*) 1949.

3098. American Society of Heating and Ventilating Engineers. Transportation air conditioning. pp. 981–996 in: *Heating ventilating air conditioning guide. 1951.* Baltimore, Waverly Press, Inc., 1951, 1456 pp.

3099. American Society of Heating and Ventilating Engineers. Instruments and measurements. pp. 1021–1040 in: *Heating ventilating air conditioning guide. 1951.* Baltimore, Waverly Press, Inc., 1951, 1456 pp.

3100. Bedford, T. Warmth and comfort. pp. 86–107 in: *Basic principles of ventilation and heating.* London, H. K. Lewis & Co., Ltd., 1948, 401 pp.

3101. Bedford, T. Stimulating and pleasant environments. pp. 115–128 in: *Basic principles of ventilation and heating.* London, H. K. Lewis & Co., Ltd., 1948, 401 pp.

3102. Crowden, G. P. and T. C. Angus. Modern views on ventilation, warming and cooling. *Practitioner,* 1947, *159:* 210–217. [R]

3103. Gt. Brit. MRC–RNPRC, CES. Review of activities. *R. N. P. 50/638, C. E. S. 335,* 23 November 1951, 7 pp.

3104. Kellogg, R. H. Critical factors in minimal air cooling of living quarters. U. S. NMRI. *Project X–205, Rept. no. 7,* 26 November 1946, 17 pp. [P]

3105. Nielsen, M. Undersøgelser over relationen mellem behagelighedsfornemmelser, opvarmningstilstand og fysiologiske reaktioner ved stillesiddende arbejde. (Studies on the relation between sensations of comfort, degree of heating and physiological reactions.) *Contribution no. 3.* Committee for the study of domestic heating, Copenhagen, 1947, 82 pp.

3106. Nielsen, M. Undersogelser over betydningen af gulvopvarmning for behagelighedsfornemmelser og fodtemperaturer. (On the importance of heating of floors for the sensation of comfort and the temperatures of the lower extremities.) *Contribution no. 4.* Committee for the study of domestic heating, Copenhagen, 1948, 28 pp. [P]

3107. Reese, J. M. The measurement of the thermal environment afloat. *J. R. nav. med. Serv.,* 1947, *33:* 200–204. [R]

3108. Yaglou, C. P. A method for improving the effective temperature index. *Trans. Amer. Soc. Heat. and Vent. Engrs.,* 1947, *53:* 307–312. [M] [R]

3109. Yaglou, C. P. Thermometry. pp. 70–77 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

3110. Yaglou, C. P. Indices of comfort. pp. 277–287 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

3111. Yaglou, C. P. Performance characteristics of BuShips footwarming panel designed for use in semi-exposed bridge areas of ships. U. S. Navy. NMRI. *Project X–189, Rept. no. 12,* 21 December 1950, 13 pp.

5. DISINFECTION OF AIR

Most airborne diseases are spread in enclosed spaces where people are in close proximity. Recent studies on air disinfection have indicated two distinct control measures: (1) suppression of dust and lint, and (2) disinfection of droplet nuclei. The control of relative humidity is also an important factor. In the submarine the suppression of dust and lint is not of prime concern because of the deterring effect on dust formation by spilled oil from machinery parts. For general studies on air disinfection, the reader should consult papers by the American Society of Heating and Ventilating Engineers (*3112*) 1951; Wolman, Fair, Hardenbergh, Lawrence, Maxcy, Tiedeman, Whittaker, and Yaglou (*3143*) 1947; and Yaglou and Wilson (*3144*) 1942. The following anonymous papers may also be consulted: (*3145* and *3146*) 1946 and 1947.

The mechanism of aerosols in aerial disinfection was discussed by Puck (*3128* and *3129*) 1947. Theoretical analysis of chemical action reveals that the rapid killing properties of aerial disinfectants can-

not be accounted for by a collision process between germicidal aerosol particles and the airborne bacteria. However, a mechanism involving condensation of germicide molecules in the vapor state on the bacteria-containing droplets results in a theoretical velocity of the correct order of magnitude. Experimental tests by the author showed that pure germicide vapors free of aerosol droplets are almost instantly lethal to airborne bacteria. Conversely, pure germicidal areosols in the absence of vapor had no effect on airborne bacteria within 20 minutes or more. Puck concluded that rapid air sterilization requires the existence of the germicide in the vapor state. According to Lester, Kaye, Robertson, and Dunklin (*3124*) 1950, minute quantities of triethylene glycol vapor (2.5 micrograms per liter of air) are sufficient to produce maximum rates of bacterial action. Relative humidity limits the maximum concentration of glycol which can accumulate within the airborne particle. The authors state that the glycol-water content of the particle should always maintain an equilibrium with the vapor concentration of these substances in the air. Humidity controls the staturation concentration according to physicochemical principles, and at high humidities the particles in equilibrium contain so much water that highly bactericidal concentrations of glycol are unattainable.

In an experiment on the efficacy of triethylene glycol for air sterilization, medical personnel at the U. S. Naval Training Center, Great Lakes, Ill. (*3140* and *3141*) 1951, treated naval barracks with this substance. Each of these barracks housed 240 to 320 persons. Epidemics of influenza, streptococcal infections, and other acute respiratory infections occurred during the experimental period. The air in the dormitories contained triethylene glycol vapor in concentrations exceeding 2.5 micrograms per liter of air. It was found that the counts of airborne bacteria were reduced approximately 65 percent in the glycol-treated barracks. Beta-hemolytic streptococci were recovered from the environment during the last 2 months of the study. No consistent reduction in acute respiratory diseases was found to occur in the 661 men living in the experimental dormitory. Additional information provided by the work of Bigg, Jennings, and Olson (*3113*) 1947 showed a 42-percent reduction of disease incidence (colds, atypical virus pneumonia, streptococcal infections, measles, mumps, etc.) in men living and working in triethylene-glycol-vapor-treated buildings.

Gedda (*3116*) 1950 published a report on the effectiveness of triethylene-glycol-vapor disinfection in an ear, nose, and throat clinic and a children's home. In the clinic waiting room the bacterial concentration of the air was reduced approximately 30 percent, and a 40-percent reduction was reported in the children's home. For related articles, the reader may wish to consult reports by Bigg, Olson, Garlock, and Jennings (*3114*) 1946; Lester, Robertson, Puck, and Wise (*3125*) 1949; Loosli, Smith, Gauld, Robertson, and Puck (*3126*) 1947; Puck and Chaney (*3130*) 1946; Robertson (*3132*) 1947; Jennings and Bigg (*3122*) 1943; Robertson, Appel, Puck, Lemon, and Ritter (*3133*) 1948; Robertson and Lester (*3134*) 1951, and Rosebury, Meiklejohn, Kingsland, and Boldt (*3137*) 1947.

Ultraviolet radiation for the control of airborne infections has been studied extensively at the Naval Training Center, Great Lakes, Ill. In these studies the floors were oiled, and oil-processed blankets were issued. Ultraviolet lamps were suspended from the ceiling and radiated upward; they were turned on 100 hours before the recruits entered the buildings. Miller, Jarrett, Willmon, Hollaender, Brown, Lewandowski, and Stone (*3127*) 1948 found that ultraviolet radiation of the floors and upper air in these barracks housing recruits resulted in a 19.2-percent overall reduction in total respiratory disease. Streptococcal disease rates were at a very high level during this particular test period, and a 24-percent reduction in rate was obtained. Followup studies by Willmon, Hollaender, and Langmuir (*3142*) 1948 covering a 4-year period showed that respiratory admission rates at sickbay, irradiated groups were consistently lower than rates from comparable control groups. Reductions as great as 20 to 25 percent were frequently observed. The authors concluded that ultraviolet radiation has a partial effect on certain types of respiratory diseases among recruits, but they caution that the results warrant continuing research.

It is quite natural to assume that men returning from leave bring pathogenic organisms aboard the submarine. Infections—especially respiratory infections—can be traced to contacts with shore-based personnel, lowered individual resistance, and inclement weather during the leave period. Quoting from one patrol report, "Ninety percent of the crew had colds due more or less to the sudden change of climate from Pearl Harbor to Dutch Harbor." The effects of ultraviolet lamps installed in the air ducts of submarines on airborne bacteria was investigated by Ingraham (*3120*) 1944. The lamps were of the low-pressure mercury-vapor type and were rated at 8 watts. Eighty percent of the emitted radiation is at the level of 2,537 Ångström units. It was found that the bacterial counts were lower with the lights

on, except in one instance of simulated submergence at the dock.

In general, the evidence does not indicate a clear-cut value of ultraviolet lighting in reducing infections of personnel in closed spaces. For other studies of the role of ultraviolet radiation in the control of airborne infections, reports by the following authors should be consulted: Coblentz (*3115*) 1942; Hama (*3117*) 1949; Hart (*3118*) 1942; Hollaender (*3119*) 1942; Jarrett (*3121*) 1949; Laurens (*3123*) 1942; Rentschler (*3131*) 1942; Robinson (*3135*) 1942; Ronge (*3136*) 1948; Scott and Locke (*3138*) 1944; and Scott and Locke (*3130*) 1945.

3112. American Society of Heating and Ventilating Engineers. Air conditioning in the prevention and treatment of disease. pp. 137–156 in: *Heating ventilating air conditioning guide. 1951.* Baltimore, Waverly Press, Inc., 1951, 1456 pp.

3113. Bigg, E., B. H. Jennings, and F. C. W. Olson. Triethylene glycol vapor distribution for air sterilization. *Trans. Amer. Soc. Heat, and Vent. Engrs.*, 1947, *53:* 397–406. [P]

3114. Bigg, E., F. C. W. Olson, F. C. Garlock, and B. H. Jennings. The control of airborne infections by the use of triethylene glycol. *Proc. cent. Soc. clin. Res.*, 1946, *19:* 67. [P]

3115. Coblentz, W. W. Standardization of ultraviolet lamps used as sources of germicidal radiation. pp. 138–141 in: *Aerobiology.* Edited by Forest Ray Moulton. American Association for the Advancement of Science. Washington, D. C., 1942, 289 pp.

3116. Gedda, E. Triethyelene glycol in air disinfection. *Abstr. World. Med.*, 1950, *7:* 561. *Nord. Med., Stockholm,* 1949, *41:* 363–371.

3117. Hama, G. M. Ultraviolet exposure from germicidal lamps. *Industr. Med.*, 1949, *18:* 75–76. [CH]

3118. Hart, D. The importance of airborne pathogenic bacteria in the operating room: a method of control by sterilization of the air with ultraviolet radiation. pp. 186–192 in: *Aerobiology.* Edited by Forest Ray Moulton. American Association for the Advancement of Science. Washington, D. C., 1942, 289 pp.

3119. Hollaender, A. Abiotic and sublethal effects of ultraviolet radiation on micro-organisms. pp. 156–165 in: *Aerobiology.* Edited by Forest Ray Moulton. American Association for the Advancement of Science. Washington, D. C., 1942, 289 pp.

3120. Ingraham, H. S. Evaluation of the bactericidal power of ultraviolet lamps on the air of the submarine U. S. S. *Angler.* With supplementary report on tests for the presence of stibine. U. S. Navy. NMRI. *Project X–45 (Sub. no. 15)*, 4 April 1944, 18 pp.

3121. Jarrett, E. T. The evaluation of ultraviolet radiation for control of airborne infections in naval barracks. U. S. Navy, Naval training center, Great Lakes, Ill., Medical research unit no. 4. *Project 005 051.01 (NM 005 008)*. 10 August 1949, 33 pp. [P]

3122. Jennings, B. H., and E. Bigg. Studies and investigations in connection with ventilating problems involved in utilization of propylene and triethylene glycol vapors for air sterilization. U. S. OSRD. Northwestern University Contract no. *OEMcmr–175, Final Rept.*, July 1943, 26 pp.

3123. Laurens, H. The physiological effects of ultraviolet radiation. pp. 142–155 in: *Aerobiology.* Edited by Forest Ray Moulton. American Association for the Advancement of Science. Washington, D. C., 1942, 289 pp.

3124. Lester, W., Jr., S. Kaye, O. H. Robertson, and E. W. Dunklin. Factors of importance in the use of triethylene glycol vapor for aerial disinfection. *Amer. J. publ. Hlth.*, 1950, *40:* 813–820. [R]

3125. Lester, W., O. H. Robertson, T. T. Puck, and H. Wise. The rate of bactericidal action of triethylene glycol vapor on micro-organisms dispersed into the air in small droplets. *Amer. J. Hyg.*, 1949, *50:* 175–188.

3126. Loosli, C. G., M. H. D. Smith, R. L. Gauld, O. H. Robertson, and T. T. Puck. Control of cross-infections in infants' wards by the use of triethelyene glycol vapor. *Amer. J. publ. Hlth.*, 1947, *37:* 1385–1398.

3127. Miller, W. R., E. T. Jarrett, T. L. Willmon, A. Hollaender, E. W. Brown, T. Lewandowski, and R. S. Stone. Evaluation of ultraviolet radiation and dust control measures in control of respiratory disease at a naval training center. *J. infect. Dis.*, 1948, *82*: 86–100.

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6. ELIMINATION OF DUST, GASES, FUMES, AND ODORS FROM AIR

In confined spaces intended for human occupancy, the processes of ventilation and air conditioning simultaneously control the moisture content, temperature, movement, and quality of air. Considering the quality of air, it is generally accepted that when the only source of contamination is the human occupant, the minimal quantity of outdoor air needed is that required to remove objectionable body odors, galley vapors, and tobacco smoke. The odor level in a space depends primarily upon a number of factors, including characteristics of the environment, dietary and hygenic habits of the occupants, the amount of outdoor air supplied, whether smoking is permitted or not, the space allowed per person, the capacity of the wet-coil cooling surface to remove odors, and the temperature and relative humidity.

Odors complained of most frequently by submarine personnel are those emanating from the waste products from the lavatories and galleys which are collected in sanitary tanks. Military security prevents emptying the tanks during hostilities, except upon surfacing under cover of darkness. The tanks are then "blown" dry with compressed air. During long patrols, despite frequent emptying and the use of various disinfectants, the tanks become unpleasantly odorous. The removal of odors from submarine air by various methods has been investigated by Consolazio and associates (*3150, 3151, 3152* and *3155*). Under conditions of mechanical cooling in conjunction with the use of activated carbon, Consolazio and Pecora (*3152*) 1947 found that the odor level for a circulation rate of 5 cu. ft. per minute per man at 78° F. effective temperature was of the same order of magnitude as that for 53 cu. ft. per minute per man for weather air. Odoriferous substances were condensed on the cooling coils and subsequently removed along with the water condensed from the air. With activated carbon, the replenishment air necessary for maintenance of an acceptable odor condition could be reduced below 5 cu. ft. per minute per man. The use of ozone did not reduce the odor level.

According to Korotianskii and Mirskii (*3157*) 1946, the soiling of air in caissons is attributable to three major factors: (1) contamination of the air by oil vapor; (2) soiling of the air as a result of the nature of work; and (3) contamination of the air by infiltration of outside natural gases (methane, carbon dioxide, etc.) from the river or sea bottom. The authors give quantitative evaluations of the methods used for air purification. The air purifiers were tested under varying conditions of pressure, temperature, and oil concentration.

McCord and Witheridge (*3162*) 1946 in their excellent text state that offensive odors unfavorably influence health only through the possibilities of lessening food and water intake, disturbing sleep, and promoting nausea and vomiting. For related articles, the reader may wish to consult reports by the American Society of Heating and Ventilating Engineers (*3147, 3148 and 3149*) 1951; Florida Chemical Research Co. (*3156*) 1950; Kuehner (*3158*) 1947; Loosli (*3159*) 1948; Luaces (*3160*) 1946; McCord (*3161*) 1952; Policard (*3163*) 1947; Ray (*3164*) 1952; U. S. National Research Council (*3165*) 1949; and Watson (*3166*) 1948.

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3165. U. S. NRC. Committee on sanitary engineering and environment. Subcommittee on shelter and clothing. Minutes of the fifth meeting, 15 November 1949, 1 p.

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7. CARBON DIOXIDE ABSORBENTS, CARBON DIOXIDE ABSORPTION, AND TOLERABLE CONCENTRATIONS OF CARBON DIOXIDE AND OXYGEN

Limiting values of carbon dioxide, after submerging without snorkel, are theoretically not attained until expiration of a period of hours calculated from the formula: $X=0.04\frac{C}{N}$ where C = net air space of tne submarine in cubic feet, N = the number of men in the crew, and X=the time in hours. If submergence under ordinary operating conditions is less than 17 hours, oxygen or compressed air replenishment and CO_2 absorption are not normally necessary. Under abnormal conditions, when the environment is damp and cold and metabolic rates are above averages, the validity of this formula may not hold. During World War II, adequate instruments to measure the concentration of carbon dioxide and oxygen in the air were not available. Need for carbon dioxide absorption was commonly based on subjective evidence, as headache, dyspnea, and failure of the air to sustain a flame. When the need became obvious, carbon dioxide absorbent, in varying amounts, was spread out on rubber mattress covers in the bunk. This haphazard procedure is entirely inadequate for submarines of advanced design and long submergence capacity.

Miller (*3175*) 1945 has reported on the experimental control of carbon dioxide aboard a U. S. Navy submarine. The atmosphere in the submarine was maintained within narrow limits at 3 percent carbon dioxide and 17 percent oxygen. The total submerged period was 68 hours. For the first 24 hours, oxygen was replenished with chlorate candles and lithium hydroxide was used for carbon dioxide absorption. During the remaining hours of submergence, the air for the 90 men was purified with KOX (potassium tetroxide). This compound reacts with carbon dioxide and water vapor to produce oxygen. Three canisters of KOX running simultaneously removed the carbon dioxide and furnished sufficient oxygen. One chlorate candle was used each 55 minutes, and oxygen was generated at the rate of 1 cubic foot per minute during the period when lithium hydroxide was used as a carbon dioxide absorbent. Both methods of air regeneration satisfied the submariners' requirements.

According to Malorny (*3173* and *3174*) 1948, the air of miniature submarines is more difficult to maintain at habitable levels than the larger fleet-type submarines. The carbon dioxide content in these small vessels is more easily maintained at safe levels (by absorbents), while the oxygen concentration is more labile because of the many individual variations in metabolic rates of the crew mem-

bers. Two methods of air purification for miniature submarines are described by the author. One method requires that crew members wear masks which absorb carbon dioxide during exhalation and permit the use of compartment air during inspiration. The oxygen supplied to the boat is either bled in from oxygen tanks or compressed air banks. The other process, not requiring the use of face masks, utilizes an air injection valve resembling that used in deep-sea diving helmets for air recirculation and carbon dioxide absorption. It is an application of the venturi principle. The energy of the oxygen or oxygen-air mixture leaving the narrow V-shaped nozzle serves to draw in the compartment air. The air mixture is then forced through a carbon dioxide absorbent.

A report by the U. S. Navy (*3178*) 1945 describes the "alka-cellulose" which replaced sodium hydroxide as a carbon dioxide absorbent on Japanese submarines. This commercial preparation, obtained by processing staple fiber, is the result of an alkalinization process. The material was packed in 4 kg. tins, and when needed the fiber was spread out on the deck. One tin of this material supposedly absorbed 400 liters of carbon dioxide. Tests of a service-type lithium hydroxide hopper for carbon dioxide removal are described by McConnaughey and Woods (*3172*) 1951. The results indicated that two such hoppers, each using about 21.6 pounds of lithium hydroxide pellets, will maintain the atmosphere in an 80-man submarine at an average carbon dioxide concentration of 1. to 1.5 percent for 4 hours without recharging. Blower requirements have been established as 75 to 85 cu. ft. per minute, at 2.5 in. of water static pressure. The reader may also care to refer to reports by the following authors: Adriani (*3167*) 1945; Davidson and Hempleman (*3168*) 1950; Foregger (*3169*) 1948; Henson and Pender (*3170*) 1944; Kindrick and Reitmeier (*3171*) 1950; Miller and Lanning (*3176*) 1941; and Mousel, Weiss, and Gilliom (*3177*) 1946.

3167. Adriani, J. The effect of varying the moisture content of soda lime upon the efficiency of carbon dioxide absorption. *Anesthesiol.,* 1945, *6:* 163–172. [P]

3168. Davidson, W. M., and H. V. Hempleman. Carbon dioxide absorption trial carried out in H. M. submarine *Trespasser,* 23rd–24th March 1950. Gt. Brit. MRC–RNPRC, UPS. *R. N. P. 50/595, U. P. S. 115,* April 1950, 5 pp.

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3170. Henson, M., and J. W. Pender. Evaluation of baralyme as a carbon dioxide absorbent. U. S. Navy. NMRI. *Project X–75,* 14 July 1944, 2 pp.

3171. Kindrick, R. C. and R. E. Reitmeier. Recommendations for the selection of amines for the absorption of CO_2 from air. U. S. Girder Corp. *Rept. no. T2. 20–2–6,* 26 July 1950, 11 pp.

3172. McConnaughey, W. E. and F. J. Woods. A pelletized lithium hydroxide hopper to remove carbon dioxide from submarine atmospheres. U. S. Navy. NRL. *NRL Rept. no. 3868,* 12 October 1951, 12 pp.

3173. Malorny, G. Investigations of compartment air in miniature submarines. Use of injector. pp. B: V–21—B: V–32 in: *Monograph on submarine medicine, Folio III,* Germany, U. S. Zone. Office of naval advisor. 1948.

3174. Malorny, G. Investigations of compartment air in miniature submarines. The significance of climatic factors. pp. B: V–36—V–37 in: *Monograph on submarine medicine, Folio III,* Germany. U. S. Zone. Office of naval advisor. 1948.

3175. Miller, R. R. Experimental control of carbon dioxide and oxygen concentrations aboard the U. S. S. *Sailfish.* U. S. Navy, NRL. *NRL Rept. no. P–2665,* October 1945, 30 pp. [P]

3176. Miller, R. R. and W. C. Lanning. The seventh partial report on oxygen source material. U. S. Navy. NRL. *NRL Rept. no. P–1691,* 4 February 1941, 20 pp.

3177. Mousel, L. H., W. A. Weiss, and L. A. Gilliom. A clinical study of carbon dioxide absorption during anesthesia. *Anesthesiol.,* 1946, *7:* 375–398.

3178. U. S. Navy, Technical mission to Japan. Carbon dioxide absorption. p. 44 in: *Aero, surface, and submarine medicine and research in the Japanese Navy, Fascile M–1, Target M–06,* 4 September 1945, 72 pp.

8. OXYGEN GENERATORS

To maintain the air of a submarine within the limits of safety, it is necessary not only to limit the increasing carbon dioxide concentration by chemical absorbents but also to replenish the decreasing supply of oxygen by adding oxygen or air at regular intervals. Future demands imposed on submarine activity by the atomic power plant will extend its submerged range beyond the limits of oxygen endurance as supplied by conventional methods.

It is not intended under this heading to include in its entirety the extensive literature on the various types and evaluation of oxygen-producing systems. A few selected reports have been included (*3183, 3185, 3187, 3188, 3191* and *3194*). Of interest is the report by Geissman (*3183*) 1946 describing the operating characteristics of "Salcomine" (salicylaldehyde ethylenediamine). This compound produced oxygen at satisfactory temperature and pressure ranges. Animal and human experiments demonstrated that the dust of "Salcomine" was irritative to the bronchial passages, digestive tract, and liver. In the 11 men exposed, the dust produced an irritation of the eyes, nose, larynx, and bronchial tubes. Removal of the men from the dust environment relieved the symptoms.

Information concerning alkali oxides for submarine air purification may be obtained from a paper by Grand, Ramskill, and Burgess (*3185*) 1942. These alkali oxide canisters were developed

for carbon dioxide absorption and oxygen generation in submarines.

In 1930, an individual oxygen generator was developed for use in mine-rescue work. This generator utilized oxygen from a chlorate briquet manufactured in Berlin under the trade name "Naszogen." The apparatus was later tested by the British Admiralty for oxygen replenishment in submarines, but was rejected because the oxygen liberated was contaminated with chlorine.

Pappenheimer (*3187* and *3188*) in 1945 published observations on the Japanese chemical oxygen generator developed for aircraft. The oxygen was evolved by the decomposition of potassium chlorate. Flow rates at 25°, −20°, and −55° C. were 4.1, 3.4, and 2.8 liters of oxygen per minute. The gas mixture produced contained 96 to 97 percent oxygen, 3 to 4 percent carbon dioxide, and 0.1 percent carbon monoxide. The blood of one observer contained 20 percent carboxyhemoglobin after 50 minutes at a simulated altitude of 18,000 feet, while the equipment supplied oxygen to the chamber. The improved candle produced in the United States contained $NaClO_3$, Fe, BaO_2, and fiberglass. The use of reduced iron as an accessory heat source diminished production of carbon monoxide and carbon dioxide. The BaO_2 eliminated the formation of free chlorine. The reader should also consult the report published by the U. S. Office of Scientific Research and Development (*3194*) 1946 for a complete bibliography on oxygen generator equipment. Other references are included without comment.

3179. Berner, F. W. Aircraft oxygen generator. U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command, ENG. *Serial no. ENG–49–660–45–I,* 6 July 1944, 4 pp.

3180. Calvin, M. Manufacture of oxygen by use of regenerative chemicals. U. S. OSRD–NDRC. Division B. *O. S. R. D. no. 403, Serial no. 186,* 23 February 1942, 10 pp.

3181. Diebold, V. B. Laboratory and flight test of the Bendix 8-liter liquid oxygen converter (Model XE795826–1), U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Serial no. MCREXD–660–104–J,* 3 March 1950, 15 pp.

3182. Dodge, B. F. The production of liquid oxygen. U. S. OSRD–NDRC. Division B. *Serial no. 59,* 14 August 1941, 36 pp.

3183. Geissman, T. A. Oxygen generation from regenerative chemicals. pp. 242–267 in: *Improved equipment for oxygen production.* Summary technical report of Division 11, U. S. OSRD–NDRC. Washington, D. C., 1946, 428 pp.

3184. Giaugue, W. F. Cascade oxygen system, U. S. OSRD–NDRC. Division B. *O. S. R. D. no. 491, Serial no. 201,* 28 February 1942, 44 pp.

3185. Grand, J. A., E. A. Ramskill, and D. S. Burgess. Eleventh partial report on oxygen source material. Use of the alkali oxides in canisters for submarine air purification. U. S. Navy. NRL. *NRL Rept. no. P–1904,* 11 July 1942, 65 pp.

3186. Latimer, W. M. The production of oxygen by the use of a regenerative chemical. U. S. OSRD–NDRC. *O. S. R. D. Serial no. 64,* 25 August 1941, 6 pp.

3187. Pappenheimer, J. R. Notes on the Japanese chemical oxygen generator for aircraft. U. S. NRC–CAM. *OEMcmr–26, C. A. M. Rept. no. 427,* April 1945, 14 pp. [P]

3188. Pappenheimer, J. R. Development of oxygen candle apparatus for use in aircraft. U. S. NRC–CAM. *C. A. M. Rept. no. 499,* June 1946, 52 pp.

3189. Prentiss, S. S. Oxygen generation from nonregenerative chemicals. pp. 268–294 in: *Improved equipment for oxygen production.* Summary technical report of Division 11, U. S. OSRD–NDRC. Washington, D. C., 1946, 428 pp.

3190. Prentiss, S. S. Liquid oxygen vaporizers for aeronautical, medical and engineering uses. pp. 295–308 in: *Improved equipment for oxygen production.* Summary technical report of Division 11. U. S. OSRD–NDRC. Washington, D. C., 1946, 428 pp.

3191. Prentiss, S. S. Submarine problems. pp. 330–342 in: *Improved equipment for oxygen production.* Summary technical report of Division 11, U. S. OSRD–NDRC. Washington, D. C., 1946, 428 pp.

3192. Rahtgen, H. G. Description and instruction for operation and maintenance of oxygen charging apparatus 10–100 3–1. U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Serial no. ENG 49–660–15–Q–1.* (German translation no. 373), 16 January 1944, 31 pp.

3193. U. S. AAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command, ENG. Aero medical laboratory. Design requirements and test results on aircraft type liquid oxygen converts. *Technical rept. TSEAL–3–660–61–J,* 25 March 1945, 21 pp.

3194. U. S. OSRD–NDRC. *Improved equipment for oxygen production.* Summary technical report of Division 11, Volume 1. Washington, D. C., 1946, 428 pp. [B]

C. BUNKING FACILITIES

There has been a lack of extensive concern for the adequacy of bunking facilities as a phase of habitability which calls for an investigation of the sleeping quarters and the type, size, and arrangements of bunks. In a standard, fleet-type submarine, enlisted personnel are provided 17 bunks in the forward torpedo room, 18 in the after torpedo room, 27 in the after battery compartment, and 5 in the chief petty officers' cabin. The bunks are only 25½ to 26 inches wide and 73 to 75 inches long. To make matters worse, some bunks are arranged in 3 or even 4 tiers, so close to each other vertically that it is impossible for a sleeper to turn over without hitting and scraping against the sagging hammock-type spring of the bunk above. Both the narrowness of the bunks and their vertical crowding discourage frequent changes in sleeping postures essential for restful sleep. Probably the absence of complaints concerning sleeping accommodations can be explained only by the esprit de corps of the

submarine service and the well-adapted type of person obtained through selection procedures.

Substitution of neoprene sponge mattresses for hair mattresses has been tried as a means of improving bunking conditions aboard submarines. An evaluation of this trial by Spealman, Trumper, Fisher, Birren, and Duggan (*3196*) 1944 showed that the neoprene mattresses were preferred to hair mattresses by 9 out of the 10 subjects, primarily because they were softer. The neoprene mattresses were not irritating to the skin nor did they absorb appreciable quantities of water during the experiment. It was recommended that a fungistatic be applied to mattresses to prevent the growth of certain fungi.

Crowded conditions, as indicated by prevailing bunking arrangements, certainly must have some effect upon the incidence of acute respiratory diseases. This problem will not be discussed here but is considered under the section on disinfection of air (p. 273). For pertinent references on this subject as applied to bunking arrangements, the reader should consult papers by the U. S. Army (*3197*) 1946 and Breese, Stanbury, Upham, Calhoun, Van Buren, and Kennedy (*3195*) 1945.

3195. Breese, B. B., J. Stanbury, H. Upham, A. J. Calhoun, R. L. Van Buren, and A. S. Kennedy. Influence of crowding on respiratory illness in a large naval training station. *War Med., Chicago,* 1945, *7:* 143–146.

3196. Spealman, C. R., M. Trumper, M. B. Fisher, J. E. Birren, and T. L. Duggan. Investigation of the suitability of neoprene sponge mattresses for use aboard submarines. U. S. Navy. NMRI. *Project X–221, Rept. no. 2,* 8 November 1944, 6 pp.

3197. U. S. Army. Commission on acute respiratory diseases. Fort Bragg, N. C. The effect of double-bunking in barracks on the incidence of respiratory disease. *Amer. J. Hyg.,* 1946, *43:* 65–81. [P]

III. FOOD AND WATER SUPPLY

When proper precautions have been taken and when the distilling machinery functions in a routine manner, water delivered to the submarine crew for drinking purposes will normally be potable. Multiple runs of the water through the distilling plant will yield salt-free water, adequate for the batteries and pure enough to drink. First consideration is given to the battery supply, while the remainder is rationed to the men for drinking, cooking, and bathing purposes. The supply for bathing is often inadequate.

During World War II a few submarines reported the occurrence of gastrointestinal symptoms among the crew which were presumed to be due to the consumption of impure drinking water. It was noticed that 2 or 3 weeks after the start of a patrol the fresh water tasted "metallic" and that cigarettes had a sweet taste when smoked after drinking the water. Some of the men developed nausea, vomiting, and malaise of varying severity. On one boat the majority of the crew was incapacitated by the symptoms and it became necessary to retire from patrol. The onset of nausea and vomiting occurred most frequently after the consumption of water in the morning before breakfast. The toxic manifestations in most cases were relieved when the men abstained from drinking water and derived their fluid intake from canned fruit juices and coffee.

At the time the drinking water developed the bad taste it was also noticed that the water turned a blue-green color when soap was added to it. This condition was reported by submarines operating in widely scattered localities—in the Gulf of Mexico, in transit from the Canal Zone to Hawaii, in the Coral Islands area, in the Inland Sea, and other parts of the Pacific Ocean.

Submarines start on a war patrol with fresh-water tanks filled with water from the dock or tender. In 1 to 3 weeks, depending on the rate of water consumption, this water is diluted 50 to 90 percent with the water distilled on board. A modern submarine during a war patrol will consume about 500 gallons of fresh water a day for cooking, drinking, and engine water makeup. In addition to this, the main storage batteries require about 500 gallons of battery water a week.

An investigation of the cause of drinking-water contamination on the U. S. S. *Icefish* by Duffner and Hayter (*3203*) 1946 revealed that the unpleasant taste of the water was due to the concentration of copper salts. The copper was found to have come from the distilling plant. The tubes in the distillation units are made of a copper-nickel alloy and over one-half of the fixed residue in the samples collected from the distillation units and from the distillate collecting tank is derived from the copper-nickel source. It is reasonably certain that these substances in the water are formed by the action of the compressed vapor and hot water on the metal tubes.

The water delivered at the crews' scuttlebutt contained approximately twice as much copper (8.18 p. p. m.) as did the water delivered at the distilling units (3.67 p. p. m.). Bacteriological examination of samples collected from each of the fresh-water tanks, the crews' scuttlebutt, the tap at the galley sink, and the distillate collecting tank did not reveal evidence of coli-aerogenes contamination.

The effect of drinking water with a copper concentration of 3 p. p. m. was investigated by Hayter and Consolazio (*3205*) in 1945. Twenty-five men drank daily for 8 days 1 pint of distilled water containing 3 p. p. m. of copper and 25 men drank this water daily for 7 days. Controls drank tap water. Seventy to eighty percent of the men noticed the taste of the copper in the water and thought it was unpleasant. One man had nausea, one had nausea with vomiting, and a third man had nausea twice and nausea with vomiting once. The authors felt that it would be advisable to keep the copper levels in the water below 3 p. p. m. This is the limit recommended by the U. S. Public Health Service for drinking and culinary water supplied by common carriers in interstate commerce.

The water supplied to the crew must be free of disease-producing bacteria. A submarine as a matter of necessity may have to distill water pumped into the boat from a foreign contaminated harbor and therefore the stills must operate at temperatures which are lethal for pathogenic bacteria. Malfunctioning of the distilling plant under these circumstances would supply the crew with contaminated water which might lead to sickness of epidemic proportions miles from home.

Payne (*3210*) 1945 carried out a very complete investigations of the bactericidal efficiency of a low-pressure, double-effect distilling plant capable of an output of 40,000 gallons per day. In all runs sufficient sewage was introduced into the feed water to produce an average probable number of coliform organisms of 605,000 per 100 cc., and an average bacterial content of 41,000 per cc. as determined by the plate count at 37° C. Results showed that the condensate was free of coliform bacteria, and the number of other bacteria was inconsequential even when highly polluted water was used. The fact that some bacteria were carried over into the condensate when the separators were removed and the salinity exceeded 0.6 grain per gallon indicates the need for efficient separators or eliminators in all plants. In cases where the eliminators are not known to be effective in keeping the salinity consistently below one-fourth grain per gallon, other means must be provided for killing the harmful bacteria. If heat is used to kill the bacteria, a minimum temperature of 165° F. is satisfactory. It was found that this temperature killed all coliform organisms, but not the more heat-resistant bacteria. In other words, a 165° F. temperature will not produce sterile water but apparently it is sufficient to kill the pathogenci bacteria.

Burrows, Gordon, Porter, and Moulder (*3201*) 1949 state that the most efficient method of killing bacteria is with dry heat. The pathogenic bacteria are less resistant to heat, the spores being more resistant and sometimes 16 hours of boiling is required to kill them. As a rule, exposure to 120° C. for 15 minutes suffices for complete destruction of both vegetative and spore forms of bacteria. Water at 100° C. for a few minutes kills all vegetative forms.

Zobell and Conn (*3221*) 1950 heated samples of sea water and mud to 30° C. for 10 minutes and found that about 25 percent of the bacteria present were killed. Only 20 percent of the bacteria survived 40° C. for 10 minutes. The authors stated that prolonged exposure at 40° to 42° C., or instantaneous exposure at temperatures a few degrees higher than 42° C., is lethal for a large percentage of the bacteria from the ocean. Marine bacteria are thermosensitive because many live at colder temperatures at the depths of the ocean. Chang (*3202*) in 1950 investigated the survival of cysts of *Entameba histolytica* in water temperatures ranging from 45 to 50° C. He found that at 45° C. for 135 minutes' contact time, approximately 115 minutes were needed to get 100 percent killing; at 47° C. for 32 minutes' contact time, 30 minutes were needed; at 49° C. with a contact time of 9 minutes, 7.5 minutes were required; and at 50° C., contact time of 3 minutes, 2 minutes were needed for 100 percent destruction. The pH of the culture was 6.8.

For other articles concerned with the general subject of water purification and testing, the reader is advised to consult reports by the following: American Public Health Association and the American Water Works Association (*3198*) 1946; Bateman (*3199*) 1943; Black and Spaulding (*3200*) 1944; Futcher, Consolazio, Pace, and Gerrard (*3204*) 1943; Jones and Newton (*3206*) 1950; Lamanna (*3207*) 1942; Moore (*3208*) 1950; Otto (*3209*) 1951; Prescott, Winslow, McCrady (*3211*) 1946; Taylor (*3213*) 1949; U. S. Public Health Service (*3217, 3218*) 1946 and (*3219*) 1951; and Zobell (*3220*) 1946.

That portion of the food problem pertaining to the preparation of foods will be alluded to briefly here, while a more thorough coverage of food as it applies to diet will be discussed in the succeeding section (p. 282). The radarange or electronic cooking device was not considered by Sussman (*3212*) 1947 to be practical for use on submarines. He listed the following disadvantages: (1) cooking is limited to a penetration of 3 inches, (2) the oven is too small, (3) the life of the magnetron

tube is too short, and (4) the timing device is defective. It was found to be superior to the standard oven in that (1) no smoke or fumes were produced during cooking, (2) there was little heat radiation, and (3) it possessed good "short-order" cooking qualities. Vegetables were found to retain their natural flavor and color. Thomas, Brenner, Eaton, and Craig (*3214*) 1949 compared the nutritive value of foods cooked on the radarange with those prepared in gas and electric ovens. They found almost no difference between the retention of nicotinic acid and of riboflavin in beef roasts or meat patties when cooked electronically and when grilled. Electronic cooking caused slightly greater loss of aneurin in beef and slightly less in patties. With electronic cooking, less ascorbic acid, riboflavin, and aneurin were retained than with pressure cooking while still less was retained with saucepan cooking. These results with vegetables are chiefly due to differences in the amount of water, most vitamins being retained with pressure cooking in which the smallest amount of water is used. For additional papers on food problems, the reader is referred to articles by the U. S. Navy (*3215*) 1949 and (*3216*) 1945.

3198. American Public Health Association and the American Water Works Association. *Standard methods for the examination of water and sewage.* American Public Health Association, New York 19, N. Y., 1946, Ninth edition—second printing (*1947*), 286 pp.

3199. Bateman, J. B. Supply of fresh water at sea. Canada NRC. Proceedings of second meeting of associate committee on naval medical research. *Project C4051,* 7 October 1943, 2 pp.

3200. Black, H. H. and C. H. Spaulding. Diatomite water filtration for field troops. *J. Amer. Wat. Wks. Ass.,* 1944, *36:* 1208–1221. [P]

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3202. Chang, S. L. Kinetics in the thermodestruction of cysts of endamoeba histolytica in water. *Amer. J. Hyg.,* 1950, *52:* 82–90.

3203. Duffner, G. J. and R. Hayter. An investigation into the cause of drinking water contamination aboard the U. S. S. *Icefish* (SS–367). U. S. Navy. NMRI. *Project X–588, Rept. no. 1,* 30 January 1946, 8 pp.

3204. Futcher, P. M., W. V. Consolazio, N. Pace, and E. J. Gerrard. The tablet emergency ration for lifeboats, rafts and floats. U. S. Navy. NMRI. *Project X–127, Rept. no. 4,* 10 November 1943, 15 pp.

3205. Hayter, R. and W. V. Consolazio. Determination of the effect of drinking water containing 3 p. p. m. copper. U. S. Navy. NMRI. *Project X–588, Rept. no. 2,* 3 May 1945, 4 pp. [P]

3206. Jones, M. F., and W. L. Newton. The survival of cysts of endamoeba histolytica in water at temperatures between 45° C. and 55° C. *Amer. J. trop. Med.,* 1950, *30:* 53–58.

3207. Lamanna, C. Relation of maximum growth temperature to resistance to heat. *J. Bact.,* 1942, *44:* 29–35. [P]

3208. Moore, E. W. The desalting of saline waters: a review of the present status. U. S. NRC. Committee on sanitary engineering and environment, Subcommittee on water supply, 24 May 1950, 13 pp. [D]

3209. Otto, G. F. Diseases and infections due to intestinal protozoa. pp. 227–242 in: *Rosenau preventive medicine and hygiene.* Edited by Kenneth F. Maxcy. Seventh edition. New York, Appleton-Century-Crofts, Inc., 1951, 1462 pp.

3210. Payne, W. W. Report of study of bactericidal efficiency of low-pressure, double-effect distilling plant. U. S. Public Health Service in cooperation with U. S. Maritime Commission. November 1945, 100 pp. [P]

3211. Prescott, S. C., C.-E. A. Winslow, and M. H. McCrady. The bacteria in natural waters. pp. 1–23 in: *Water bacteriology. With special reference to sanitary water analysis.* Sixth edition. New York, John Wiley & Sons, Inc., 1946, 368 p. [P]

3212. Sussman, L. Evaluation of electronic cooking device (radarange) for submarines. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 011 016,* October 1947, 17 pp.

3213. Taylor, Edwin Windle. The examination of waters and water supplies. London, J. & A. Churchill, Ltd., 1949. Sixth edition, 819 pp.

3214. Thomas, M. H., S. Brenner, A. Eaton, and V. Craig. Effect of electronic cooking on nutritive value of foods. *J. Amer. diet. Ass.,* 1949, *25:* 39–45. *Abstr. World Med.,* 1949, *6:* 138.

3215. U. S. Navy. BuNavPers. Analysis of submarine food problems in World War II. pp. 165–174 in: *Submarine medicine practice. NavPers. 10838,* March 1949, 182 pp. [D]

3216. U. S. Navy, Technical mission to Japan. Rations for submarine crews. pp. 41–42 in: *Aero, surface, and submarine medicine and research in the Japanese Navy, Fascile M–1, Target M–06,* 4 September 1945, 72 pp.

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3218. U. S. Public Health Service. Manual of recommended water-sanitation practice. *Public Health Bulletin no. 296,* U. S. Government Printing Office, Washington, D. C., 1946, 40 pp.

3219. U. S. Public Health Service. Potable water. pp. 1–20 in: *Handbook on sanitation of vessels in operation.* PHS publication no. 68, U. S. Government Printing Office, Washington, D. C., 1951, 44 pp.

3220. ZoBell, Claude E. Characteristics of marine bacteria. pp. 114–128 in: *Marine microbiology. A monograph on hydrobacteriology.* Waltham, Mass., Chronica Botanica Co., 1946, 240 pp.

3221. ZoBell, C. E. and J. E. Conn. Studies on the thermal sensitivity of marine bacteria. *J. Bact.,* 1950, *40:* 223–238.

IV. DIET AND PHYSICAL FITNESS

There is at present very little nutritional research directly involving submariners and therefore the dietary problems of submarine personnel must be projected onto the general background of available nutritional knowledge. Since there are few events

in his daily routine besides his meals to which the submariner really looks forward, he is likely to indulge in excessive eating. This habit, in addition to the possible immediate effects of reducing alertness and capacity to concentrate on complex tasks may permanently affect dietary practices.

Ordinarily physicians are not greatly concerned with the details of food supplies. The naval medical officer is specifically charged with the duty of "inspecting, as to quality, all fresh provisions issued as authorized mess". A review of the patrol reports by Shilling and Duff (*3226*) 1947 and (*3227*) 1948 indicated that this duty too often was not assumed by medical officers associated with the submarine force. It was recommended by the authors that submarine squadron medical officers should actively concern themselves not only with the quality of food issued to submarines but with the planning of menus to provide a dietetically acceptable ration. This should be accomplished by close cooperation of the medical staff officers, commissary personnel, and commanding officers.

The ration provided a submarine must fulfill certain requirements. It must occupy a minimum space and must evidence excellent keeping qualities in stowage. From it a daily well-balanced menu incorporating a maximum of food value and variety and a minimum of waste should be easily prepared. Submarines have always had a more generous ration allowance than other ships or stations with a similar complement.

Indication of the role which food supplies may have in influencing the length and success of patrols is shown by reports of commanding officers. "Food supply was low; the decision to remain on station was based on a 5-day supply of food. The patrol could not have continued for a longer period without a serious reduction in efficiency and health due to an unbalanced ration". "The ice cream freezer paid for itself many times over, it being estimated that one ton of ice cream was consumed during the patrol, cold weather notwithstanding".

Meat—its quality and quantity—was the one article of the submarine ration commented upon most frequently, according to Shilling and Duff. Early in the war, for reasons of space economy, boneless beef was made available to submarines. It was supplied as steak and roasting, stewing and boiling, and chopped beef. Regulations of the Bureau of Supplies and Accounts for all ships required that 30 percent of the meat was to be drawn in inferior quality. Submarines starting on patrol were issued beef in the following proportions: (1) roast and steaks 50 percent; (2) hamburger 25 percent; and (3) stewing and boiling meat 25 percent. The result of such a situation evoked the following comments in one of the patrol reports: "This is a satisfactory proportion but since stewing and boiling meat is not considered worth the icebox space, it is generally left at the base and other frozen items, as shrimps, frozen foods, and sausage are taken in quantity to fill the space." Duff and Shilling recommended that this entire problem be restudied in a less hurried atmosphere with the view toward constructing a master ration plan for the submarine service, sufficiently exact to be helpful as a guide and at the same time flexible enough to allow for satisfying individual preferences.

An excellent review of nutritional problems in submarines by Brozek and Mickelsen (*3222*) 1949 indicates that physiologically no acute nutritional problems exist as far as the submarine personnel are concerned. The requirements for calories, vitamins, minerals, proteins, carbohydrates, and fats appear to be the same as those of other moderately active men. Consequently, improvement in submarine nutrition depends on general progress in the physiological understanding of the role of food in the overall metabolism of the human organism and on technological developments of food growing, preservation, and preparation. There is a gap in our knowledge of the changes occurring, during prolonged patrols, in food preferences, likes, and dislikes, and the overall position of food in the life of the submarine personnel. When men are subjected to confining and trying circumstances, some of them may find an escape in eating. On the other hand, nervousness and anxiety may result in a loss of appetite.

Schulte (*3225*) 1950 found that 3,800 calories per man per day were consumed by submariners in a simulated war patrol in the arctic zone and this was supplied by 120 grams of protein, 480 grams of carbohydrate and 120 grams of fat. The ingested diet contained more than the established minimum adult requirements of thiamin, riboflavin, ascorbic acid, and vitamin A. From this patrol it was determined that the consumption by this crew was not appreciably greater or less than the nutritional requirements since there were no significant weight changes.

For further studies on food and physical fitness, reference may be made to reports by Dugal, Leblond, Therien (*3223*) 1945 and Ellis (*3224*) 1948.

3222. Brozek, J. and O. Mickelsen. Diet. pp. 311–327 in: *A survey report on human factors in undersea warfare.* National research council. Washington, D. C. 1949, 541 pp.

3223. Dugal, L. P., C. P. Leblond, and M. Therien. Resistance to extreme temperatures in connection with different diets. *Canad. J. Res.*, 1945, *23* (E–F): 244–258.

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3225. Schulte, J. H. A dietary study of a submarine patrol in the arctic. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM 002 015.06.01, Rept. no. 1,* 1950, 33 pp.

3226. Shilling, C. W. and I. F. Duff. Analysis of submarine food problems in World War II. pp. 215–241 in: *History of submarine medicine in World War II.* Edited by Shilling, C. W. and J. W. Kohl. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory, 25 May 1947, 328 pp.

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V. CLOTHING

A. GENERAL STUDIES

The references that follow provide a general introduction to the problems of clothing under a wide variety of environmental conditions.

3228. Burton, A. C. Clothing and heat exchanges. *Fed. Proc. Amer. Soc. exp. Biol.*, 1946, *5:* 344–351. [R]

3229. Critchley, M. Problems of naval warfare under climatic extremes. Lecture I. *Milit. Surg.*, 1946, *98:* 94–106. [R]

3230. Gagge, A. P. Research on military clothing. U. S. NRC–CAM. *C. A. M. rept. no. 39,* 5 January 1942, 4 pp.

3231. Gt. Brit. MRC–RNPRC. Special meeting clothing panel. *C. P. rept. no. 6,* 18 January 1951, 3 pp.

3232. Lee, D. H. K. and H. Lemons. Clothing for global man. *Geogr. Rev.*, 1949, *39:* 181–213. [R]

3233. Robinson, S. and H. S. Belding. Protective clothing. pp. 497–519 in: Part IV Physiology in: *Advances in military medicine. Vol. II.* Edited by E. C. Andrus, D. W. Bronk, G. A. Carden, Jr., C. S. Keefer, J. S. Lockwood, J. T. Wearn, and M. C. Winternitz. Boston, Little, Brown and Co., 1948, 472 pp. [R]

3234. Siple, P. A. Clothing and climate. pp. 389–442 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

3235. U. S. Navy. BuMed. Naval clothing. pp. 65–91 in: *A manual of naval hygiene.* U. S. Government Printing Office, Washington, D. C., 1943, 340 pp.

3236. U. S. NRC. Subcommittee on clothing. Minutes of the third meeting. 17 June 1943, 16 pp.

3237. U. S. NRC. Subcommittee on clothing. Minutes of the fourth meeting on jungle clothing. 6 October 1943, 12 pp.

3238. U. S. NRC. Subcommittee on clothing. Minutes of the seventh meeting. 15 December 1943, 8 pp.

3239. U. S. NRC. Subcommittee on clothing. Minutes of the meeting. 10 March 1944, 6 pp.

3240. U. S. NRC. Subcommittee on clothing. Minutes of the meeting. 6 May 1944, 14 pp.

3241. U. S. NRC. Subcommittee on clothing. Minutes of conference on climatic stresses. 9 March 1945, 11 pp.

3242. U. S. NRC. Subcommittee on clothing. Minutes of conference on climatic stresses. 16 April 1945, 4 pp.

3243. U. S. NRC. Subcommittee on clothing. Minutes of meeting. 19 June 1945, 10 pp.

3244. U. S. NRC. Subcommittee on clothing. Minutes of meeting. 24 October 1945, 22 pp.

3245. U. S. NRC. Subcommittee on shelter and clothing. Committee on sanitary engineering and environment. Medical advisory commission. Minutes of first meeting. Bulletin, shelter and clothing, 1 June 1948, 5 pp.

3246. U. S. NRC. Subcommittee on shelter and clothing. Commission on sanitary engineering and environment. Medical advisory commission. Minutes of third meeting. Bulletin, shelter and clothing. 17 June 1949, 9 pp.

B. PHYSICAL PROPERTIES, TESTING, AND STANDARDS

With the advent of the newer types of submarines where streamlining leaves little protection for bridge personnel, the need for more effective protection of watchstanders on the bridge becomes pressing. In rough seas and cold weather, the physical tolerance of watchstanders is limited, the periods sometimes being as short as 30 minutes. To keep men dry, when waist-deep seas are encountered, something comparable to a diving suit is required; and the solution is made more difficult by the special needs of the submarine service, in that not only is adequate protection required, but maximum mobility must be maintained for such actions as clearing the bridge under emergency conditions.

For general references on the subject of physical properties, testing, and standards of clothing, papers by the following should be consulted: Bartell, Purcell, and Dodd (*3248*) 1943; Burton (*3255*) 1948; Coke, Kitching, and Page (*3256*) 1944; Christensen (*3257*) 1948; Fourt and Harris (*3261*) 1949; Fourt and Parrish (*3262*) 1945; Goodings, Coles, Kitching, Burton, Coke, and Bazett (*3264*); Herrington (*3266*) 1945; Lee, White, and Kelso (*3269*) 1945; Newburgh and Harris (*3272*) 1945; and Perry (*3273*) 1949. Fourt and Harris limit their discussion of clothing fabrics to those properties relating to human comfort and efficiency, e. g., effects of fabrics on the passage of air, heat, and water vapor. When a large amount of insulation is needed, a quilted combination shows superior thermal effectiveness per unit of weight. The surface characteristics determining the warm or cool feel of fabrics is the result of rapid local cooling of the skin by drawing heat into the fabric. Since fabrics do not differ greatly in their specific heats, this effect depends on the fraction of gross surface which is in actual contact and the mass of fibres behind it. Therefore, fabrics woven of filament yarns and linen, with their long straight fibres, tend to feel cooler than the more hairy cotton fabrics, while wool

with its springy, hairy surface feels warmest of all. The authors (*3261*) stress the important relationship between the absorption capacity of clothing and water vapor.

Regarding the transfer of heat to the environment by fabrics and the thermal insulation of ambient air, a number of studies have been reported which are contributory. For such studies, papers by the following should be consulted: Barker (*3247*) 1951; Blum (*3250*) 1945; Burton (*3253* and *3254*) 1945; Fetcher, Rapaport, Hall, and Shaub (*3259*) 1949; Forbes (*3260*) 1949; Herrington (*3267*) 1947; Mendelson, Hosbach, Libet, and Bazett (*3270*) 1945; Wulsin (*3286*) 1945; and Yaglou (*3287*) 1945. Burton (*3253*) points out that the clo determination of the insulating value of clothing depends on the knowledge of the amount of heat passing through the clothing via radiation and convection. The heat debt is equal to the thermal capacity of the body times the fall of body temperature. It is recommended that a specific heat value of 0.83 for the body be used until further experimental determinations on the whole human body suggest another value.

Yaglou (*3287*) 1945 cautions the researcher against the unlimited use of insulation value formulas for the estimation of protection afforded by low temperature clothing assemblies because the overall figure gives no idea of protection of those areas particularly sensitive to cold, such as the shoulders, back, hands, knees, and feet. Inadequate protection of these critical areas greatly reduces endurance to cold. A method is described for evaluating local insulation of critical areas, as well as insulation of individual articles of clothing.

For further studies on thermal insulation provided by clothing, papers by the following should be consulted: Belding, Darling, Griffin, Robinson, and Turrell (*3249*) 1945; Burton (*3251*) 1943 and (*3252*) 1944; Herrington (*3265*) 1945; Rinecker (*3274*) 1950; Siple (*3275* and *3276*) 1945; U. S. National Research Council (*3281*) 1944; (*3282*) 1945; and (*3283*) 1948; Winslow (*3285*) 1949; and Yaglou (*3289* and *3290*) 1948.

For papers concerning special problems of clothing design, papers by the following may be consulted: Debons (*3258*) 1950; Law, Wright, and Gotlieb (*3268*) 1950; Talbot (*3277, 3278* and *3279*) 1945; U. S. National Research Council (*3280*) 1942; Van Dilla, Day, and Siple (*3284*) 1949; and Yaglou (*3288*) 1946.

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3249. Belding, H. S., R. C. Darling, D. R. Griffin, S. Robinson, and E. S. Turrell. Evaluation of thermal insulation provided by clothing. pp. 9–21 in: *Clothing test methods,* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3250. Blum, H. R. Solar heat load. pp. 23–36 in: *Clothing test methods.* Edited by L. H. Newburg and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3251. Burton, A. C. The use of the "table of wind chill values" prepared by the climatic research unit. Canada NRC–ACAMR. *A. C. A. M. R. rept. no. C 2454, S. P. C. 115,* 5 April 1943, 2 pp.

3252. Burton, A. C. Standard values for the thermal insulation of ambient air with different degrees of air movement. Canada NRC–ACAMR. *A. C. A. M. R. rept. no. C 2753, S. P. C. 185,* 16 November 1944, 5 pp.

3253. Burton, A. C. Calculation of the heat debt. pp. 5–7 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

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3255. Burton, A. C. On the science of field testing as applied to clothing and personal equipment. University of Western Ontario, Canada, 1948, 31 pp.

3256. Coke, C. E., J. A. Kitching, and E. Page. Disposal of body moisture in subjects wearing various types of exposure suits. Canada NRC–ACAMR. *A. C. A. M. R. rept. no. C 2689, S. P. C. 165,* 18 May 1944, 8 pp. [P]

3257. Christensen, W. R. Effects of physical characteristics of fabrics upon physiological heat load and subjective reactions. *J. industr. Hyg.*, 1948, *30:* 251–255.

3258. Debons, A. Gloves as a factor in reduced dexterity USAF. Ladd air force base, Alaska. Arctic aeromedical laboratory, Alaska. *Project no. 21–01–018,* February 1950, 6 pp. [P]

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3261. Fourt, L. and M. Harris. Physical properties of clothing fabrics. pp. 291–319 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp. [P]

3262. Fourt, L. and M. E. Parrish. Quamco cloth (bonded silica aerogel fabrics). U. S. NRC-CAM. *OEMcmr–506, C. A. M. rept. no. 459,* July 1945, 2 pp. Abstr. [P]

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by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3264. **Goodings, A. C., B. C. Coles, J. A. Kitching, A. C. Burton, C. E Coke, and H. C. Bazett.** Investigation of physiological factors influencing water loss from the body and humidity of clothing. Canada NRC-ACAMR. *A. C. M. R. rept. no. 114,* no date, 6 pp.

3265. **Herrington, L. P.** Measurement of skin and clothing temperatures. p. 3 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3266. **Herrington, L. P.** Moisture loss and moisture evaporated. pp. 21–22 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

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3269. **Lee, D. H. K., C. White, and W. T. Kelso.** Studies of evaporation from an artificial "skin" underneath service cloths. Australia, NHMRC, Fatigue laboratory, University of Queensland. *Report no. 2,* 27 September 1945, 4 pp. [P]

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3273. **Perry, W. O.** Development of insulating cloth for cold weather clothing. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Technical rept. 5753,* January 1949, 5 pp. [P]

3274. **Rinecker, F. G.** Thermal characteristics of multilayer combinations of aluminum foil and nylon and cotton fabric in clothing. USAF. Wright-Patterson air force base, Dayton, Ohio. Air materiel command. *Serial no. MCREXD–666–23H,* 16 August 1950, pp. 5.

3275. **Siple, P.** Definition of adequacy of clothing in cold climates. pp. 65–72 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3276. **Siple, P. A.** General principles governing selection of clothing for cold climates. *Proc. Amer. phil. Soc.,* 1945, *89:* 200–234. [R: P]

3277. **Talbott, J. H.** Standardization of subjects. pp. 41–45 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3278. **Talbott, J. H.** Tolerance time. pp. 47–48 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3279. **Talbott, J. H.** Grading of sensation. pp. 49–50 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3280. **U. S. NRC.** Subcommittee on clothing. Minutes of first meeting. 17 June 1942, 14 pp.

3281. **U. S. NRC.** Subcommittee on clothing. Minutes of the meeting. 13 September 1944, 7 pp.

3282. **U. S. NRC.** Subcommittee on clothing. Minutes for meeting January 26, 1945, 4 pp.

3283. **U. S. NRC.** Subcommittee on shelter and clothing. Minutes of second meeting: (Insulation characteristics of fibrous glass lined garments), 30 November 1948, 14 pp.

3284. **van Dilla, M., R. Day, and P. A. Siple.** Laboratory and field studies. Special problem of hands. pp. 374–388 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp.

3285. **Winslow, C.-E. A. and L. P. Herrington.** The thermal protective influence of clothing. pp. 116–162 in: *Temperature and human life.* Princeton, Princeton University Press, 1949, 272 pp. [P]

3286. **Wulsin, F. R.** Metabolic rates for military activities. pp. 51–61 in: *Clothing test methods.* Edited by L. H. Newburgh and Milton Harris. Ann Arbor, Michigan, Edwards Brothers, Inc., 1945, 325 pp.

3287. **Yaglou, C. P.** A rational method for determining local and overall insulation of low temperature clothing. U. S. Navy. NMRI. *Rept. no. 8, Project X–189,* 19 September 1945, 8 pp.

3288. **Yaglou, C. P.** Pressures in the interior of army footgear. *Report to the Office of the Quartermaster General,* 21 January 1946, 10 pp. [P]

3289. **Yaglou, C. P.** Thermal insulation and comfort characteristics of fibrous glass-lined garments. *J. Industr. Hyg.,* 1948, *30:* 312–315. [P]

3290. **Yaglou, C. P.** Thermal insulation of clothing. *Trans. Amer. Soc. Heat, and Vent. Engrs.,* 1948, 54: 291–298. [R]

C. EFFECTS OF CLOTHING ON PHYSIOLOGICAL RESPONSES TO ENVIRONMENTAL CHANGES

Physiological adjustments to sudden changes in ambient environment of 7 subjects wearing standard summer weight clothing compared with subjects wearing cotton, full length union suits were investigated by Glickman, Inouye, Keeton, Telser, and Fahnestock (*3292*) 1950. Exposure for one hour in a comfortable room at 24.4° C. with a vapor pressure of 9.2 and 24.4 kilodynes per sq. cm. was followed by 1 or 2 hours in the hot room at 37° C. with a vapor pressure of 41.1 kilodynes per sq. cm. Only slight differences in the physiological adjustments of the subjects was noted, these occurring primarily during the first 10 minutes of exposure. The buffering effect of clothing was evident on entering the hot room. Greater pulse rate increases were noted in the subjects wearing full length union suits during the first hour of exposure.

Fourt (*3294*) 1949 states that summer clothing should possess good "wetting out" characteristics so that "blobs" of sweat can be spread out over large

clothing areas for rapid evaporation. The author also believes that individual sweat glands may alternate in activity and that there is "hunting around" for the optimal rate of heat loss.

The effect of body warmth, foot exercise, and surrounding insulation on foot comfort in cold water was investigated by Spealman (*3298* and *3299*) 1944. The author concluded that when the body is cold, large amounts of insulation will not maintain the feet at a temperature greatly above that at which immersion foot is known to occur. On the basis of the information obtained under conditions where the body is warm, it appears that measures for conserving body heat are of greater importance in maintaining elevated foot temperatures than is local insulation. Foot exercise also helped to maintain adequate foot temperatures when the feet were insulated (cellular rubber).

For further reports on clothing in relation to physiological adjustments to environmental changes, papers by the following should be consulted: Belding, Russell, Darling, and Folk (*3291*) 1947; Folk and Peary (*3293*) 1951; Griffin, Folk, and Belding (*3295*) 1944; Horvath (*3296*) 1948; Lifson and Visscher (*3297*) and U. S. National Research Council (*3300*) 1942.

3291. Belding, H. S., H. D. Russell, R. C. Darling, and G. E. Folk. Analysis of factors concerned in maintaining energy balance for dressed men in extreme cold; effects of activity on the protective value and comfort of an arctic uniform. *Amer. J. Physiol.,* 1947, *149:* 223–239.

3292. Clickman, N., T. Inouye, R. W. Keeton, S. E. Telser, and M. K. Fahnestock. The effect of clothing on the physiological adjustments of human beings to sudden change in environment. *Fed. Proc. Amer. Soc. exp. Biol.,* 1950, *9:* 48.

3293. Folk, G. E. and R. E. Peary. Penetration of water into the human foot. U. S. Army. Office of the Quartermaster General. Lawrence, Mass. Quartermaster climatic research laboratory. Environmental protection section. *Rept. no. 181,* October 1951, 44 pp. [R]

3294. Fourt, L. Effect of clothing on heat exchange of man in hot environments. pp. 14–16 in: U. S. NRC–CAM. *Conference on acclimatization.* 17 June 1949, 29 pp.

3295. Griffin, D. R., G. E. Folk, and H. S. Belding. Physiological studies of exposure suits in hot and cold environments. U. S. OSRD–CMR. Harvard fatigue laboratory, Harvard University. *OEMcmr 54 and 328, Rept. no. 26,* 9 March 1944, 4 pp. [P]

3296. Horvath, S. M. Ventilation of clothing and tolerance of man to low environmental temperatures. J. industr. Hyg., 1948, *30:* 133–139. [P]

3297. Lifson, N., and M. B. Visscher. Effect of wet garments on body weight loss at high environmental temperatures. U. S. NRC. Committee on clinical investigation. No date, 7 pp. [P]

3298. Spealman, C. R. The relationship between foot temperature and amount of insulation surrounding the foot immersed in cold water. U. S. Navy. NMRI. *Project X–297, Rept. no. 2,* 11 March 1944, 6 pp. [P]

3299. Spealman, C. R. The effect of body warmth and foot exercise on the temperature of feet immersed in ice water. U. S. Navy. NMRI. *Project X–297, Rept. no. 4,* 28 August 1944, 5 pp.

3300. U. S. NRC. Subcommittee on clothing. Minutes of the second meeting. 10 August 1942, 32 pp.

D. CLOTHING FOR COLD AND DRY CONDITIONS

The lack of adequate protection for watch standers on the bridge of the newer type submarines exposes these personnel to heavy, cold seas. References in this section have been included because they provide clothing data which may be applied to clothing research where conditions of cold, wet environments will be encountered.

3301. Bearn, F. A. Clothing for war in arctic climates: experiences in Iceland. *Inter-allied conferences on war medicine. 1942–1945,* published 1947: 282–283.

3302. Belding, H. S. Protection against dry cold. U. S. Army. Office of the Quartermaster General. Lawrence, Mass. Quartermaster climatic research laboratory. Environmental protection section. *Rept. no. 155,* 2 August 1949, 19 pp.

3303. Blair, E. A. and C. W. Gottschalk. Efficiency of signal corps operators in extreme cold. U. S. Army. Fort Knox, Kentucky. Armored medical research laboratory. *Project 57,* 22 January 1947, 17 pp. [P]

3304. Busby, J. C. and S. V. Gianola. Arctic clothing for naval personnel. A report to the chief of Bureau of Supplies and Accounts on the work of the arctic clothing expedition at Point Barrow, Alaska, 12 October 1948 to 30 April 1949. U. S. Navy, Naval clothing depot, Brooklyn, New York. 1 May 1949, 123 pp.

3305. Critchley, M. Medical observations during passage on northern convoy; in Russia; and in Iceland. Gt. Brit. MRC–RNPRC, CES. *R. N. P. 48/454, C. E. S. 251,* May 1948, 53 pp.

3306. Gt. Brit. MRC–RNPRC, CES. Clothing panel. (Summary of R. N. P. 49/564 'Observations on physiological and clothing problems in the arctic during Operation "Rusty" ', by C. H. Wyndham and W. G. Wilson-Dickson). (Revision of C. P. 4). *C. E. S. 332, C. P. 4* (*A*), 23 November 1951, 5 pp. [D]

3307. U. S. Navy. BuY&D. Report on arctic clothing experience. *NavDocks P–13,* May 1948, 29 pp. [D]

3308. Anon. Footwear for frigid feet. U. S. Navy. ONR. *Res. Rev.,* March 1951, pp. 7–8.

E. PROTECTIVE CLOTHING FOR IMMERSION AND RAIN

The clothing requirements of immersion suits for aviators and cold weather deck clothing for submarine personnel are quite similar. The protective clothing must be water-tight for immersion in water or exposure to heavy seas, must possess qualities of warmth, and must be durable enough to resist tearing against bridge gear in heavy seas, and trim enough to fit through small hatches.

An exposure suit tested for shipboard use by Margolis (*3316*) 1946 was found to be satisfactory for immersion in sea water ranging in temperature

between 28° and 48° F. The suit is made of a water-impermeable laminated fabric composed of two plies of olive drab cotton sheeting with a waterproof coating between the layers. It envelops the body up to the neck and is seated by a drawstring. The sleeves have an extra cuff of rubber and standard Navy boots are cemented and sewed to the legs.

Concerning the protective properties of clothing for subjects immersed in cold water, Newburgh and Spealman (*3318* and *3319*) 1943 found that the rate of cooling was greatly retarded when dry clothing was worn underneath the watertight suit. The nude subject enclosed in the watertight suit cooled as quickly as the entirely naked man.

For further studies on immersion suits and water repellent clothing, reference may be made to the following reports: Cowan and Grant (*3309*) 1944; Fonash (*3310*) 1947 and (*3311*) 1949; Bazett (*3312*) 1942; Gerking and Robinson (*3313*) 1945; Gerking, Robinson, and Turrell (*3314*) 1944; Lombard and Creedon (*3315*) 1946; Murrell (*3317*) 1951; Pugh (*3320*) 1951; Spealman and Margolis (*3321*) 1945; and U. S. Navy, BuNavPers (*3322*) 1949.

3309. Cowan, C. R. M. and R. Grant. Royal Canadian Navy participation in clothing trials. Canada NRC. Proceedings of third meeting of associate committee on naval medical research. *Project C4077,* 15 May 1944, 3 pp. [P]

3310. Fonash, R. L. Test and evaluation of four experimental modifications of the MK 2 exposure suit. U. S. Navy. Aero medical laboratory, Philadelphia, Penna. *Rept. TED no. NAM 2574–.4,* 15 October 1947, 11 pp. [P]

3311. Fonash, R. L. Test and evaluation of four experimental modifications of the MK 2 exposure suit. U. S. Navy. Air materiel center, Philadelphia, Penna. Aeronautical medical equipment laboratory. *Rept. TED no. NAM 25704.4, BuAer ltr Aer–AE–52, 08474,* 30 June 1949, 11 pp.

3312. Bazett, H. C. Watertight suits. Canada NRC–ACAMR. *A. C. A. M. R. rept. no. C 2339, S. P. C. 59,* 19 October 1942, 3 pp.

3313. Gerking, S. D. and S. Robinson. Physiological comparisons of water repellent and water absorbent clothing. U. S. NRC–CAM. *OEMcmr–351, C. A. M. rept. no. 432,* 24 April 1945, 7 pp.

3314. Gerking, S. D., S. Robinson, and E. S. Turrell. A physiological study of raincoats and ponchos. U. S. OSRD–CMR. *Contract no. OEMcmr–351, Interim rept. no. 13,* 17 July 1944, 10 pp.

3315. Lombard, B. F. and W. E. Creedon. Evaluation of exposure suits designed and manufactured by H. K. Shaw. U. S. Coast Guard. Field testing and development unit. A Coast Guard Yard, Curtis Bay, Md. *Project CGTD–55–02–45, Rept. no. 1,* 1 October 1946, 31 pp. [P]

3316. Margolis, S. I. Field trial of an exposure suit for shipboard use. U. S. Navy. NMRI. *Project X–189, Rept. no. 10,* 26 June 1946, 4 pp.

3317. Murrell, H. Job classification of naval activities undertaken above deck. Gt. Brit. MRC–RNPRC. Departments of operational research and of the senior psychologist. *Naval motion study unit report no. 44,* September 1951, 7 pp.

3318. Newburgh, L. H. and C. R. Spealman. Protective clothing for subjects immersed in cold water. U. S. Navy. NMRI. *Project X–189, Rept. no. 1,* 10 July 1943, 4 pp.

3319. Newburgh, L. H. and C. R. Spealman. Protective clothing for subjects immersed in cold water. Part A. Some characteristics of the "Paske" suit. Part B. Degree of protection against evaporating cooling afforded by water-tight suits. U. S. Navy. NMRI. *Project X–189, Rept. no. 2,* 10 August 1943, 5 pp.

3320. Pugh, L. G. C. Summary of physiological observations during operation "Rusty", with particular reference to clothing. (Revision of C. P. 3). Gt. Brit. MRC–RNPRC, CES. *C. E. S. rept. 334, C. P. 3(a),* 23 November 1951, 5 pp.

3321. Spealman, C. R. and S. I. Margolis. Comparative comfort of the combination rain suit-exposure suit (Red Star Rubber Co.) and Navy Parka Rain Clothing. U. S. Navy. NMRI. *Project X–189, Rept. no. 9,* 29 October 1945.

3322. U. S. Navy. BuNavPers. (A) Submarine clothing. pp. 175–176 in: *Submarine medicine practice NavPers 10838,* March 1949, 182 pp. [D]

F. CLOTHING FOR CONDITIONS OF HEAT AND HUMIDITY

Experiments carried out by Yaglou and Rao (*3328*) 1947 on men, wearing loose and close-fitting clothing exposed to a chamber temperature of 85° F. with a relative humidity of 85 percent and an air movement of 70 feet per minute, demonstrated that the loose-fitting clothing was more comfortable under these conditions. The subjects felt that it was more comfortable because when the loose clothing became wet it did not stick to the skin as much as the close-fitting clothing.

Shelley, Eichna, and Horvath (*3326*) 1946 investigated the effects of two types of clothing on the ability of acclimatized men to work at upper heat limits. The upper limiting wet bulb temperature for successful group performance of four hours marching at three miles per hour (dry bulb temperature, 120° F.) was 92° F. for nude men, 90° F. for men wearing herringbone twill, and 88° F. for men wearing impregnated herringbone twill uniforms. At upper limits of environmental heat, wearing of a single layer herringbone twill uniform (8 ounces) imposes a heat load which is equivalent to a 2° F. increase in wet bulb temperature.

Robinson (*3325*) 1945 states that the physiological difference between the hottest and coolest suit is much less than the difference between the coolest suit and shorts. When the subjects wore shorts, skin temperature, sweating and heart rates were lower. The actual amount of sweat evaporated was less when the subjects wore shorts, suggesting that the efficiency of evaporation in cooling the body may

be greater when it takes place directly from the skin than when it takes place from clothing surfaces.

For reports on clothing under conditions of heat and humidity, reference may be made to papers by Buettner and Richey (*3323*) 1951, Gerking and Robinson (*3324*) 1945, and U. S. National Research Council (*3327*) 1943.

3323. Buettner, K. and E. O. Richey. Effects of extreme heat on man. IV. Mechanism of heat transfer in an open gasoline fire. USAF. Randolph Field, Texas. School of aviation medicine. *Project 21–26–002, Rept. no. 4,* July 1951, 4 pp.

3324. Gerking, S. D. and S. Robinson. The physiological effects of double layers of cloth on summer flying suits. U. S. OSRD. *Contract no. OEMcmr 351, interim rept. no. 23,* 19 February 1945, 3 pp. [P]

3325. Robinson, S. Laboratory and field studies. Tropics. pp. 338–351 in: *Physiology of heat regulation and the science of clothing.* Edited by L. H. Newburgh. Philadelphia, W. B. Saunders Co., 1949, viii, 457 pp. [P]

3326. Shelley, W. B., L. W. Eichna, and S. M. Horvath. The effect of clothing on the ability of men to work in intense heat. *J. clin. Invest.,* 1946, *25:* 437–446.

3327. U. S. NRC. Subcommittee on clothing. Minutes of the second meeting on jungle clothing. 19 August 1943, 3 pp.

3328. Yaglou, C. P. and M. N. Rao. Loose versus close-fitting clothing for work in "tropical heat". *J. industr. Hyg.,* 1947, *29:* 140–142. [P]

VI. DEEP SEA DIVING EQUIPMENT AND PROCEDURES

Diving with apparatus is usually considered by the layman to be divided into deep sea and shallow water diving, the distinction being made in terms of depth. These two terms have been used so frequently that the whole subject of diving has popularly come to be divided into these two categories. Deep sea diving has tended to imply diving to more than 36 feet with shallow water diving referring to diving to less than 36 feet. In diving, the type of work to be undertaken, location of the work, the extent of the operations, and the climatic conditions, in addition to depths, are the determining factors in deciding upon the personnel and type of equipment to be used and the method of accomplishing the task. Therefore, the distinction between deep sea and shallow water diving is not a sharp one. For reasons of convenience the present section deals with diving in which the respiratory gas mixture is supplied to the diver from surface equipment. The discussion of self-contained diving apparatus is included in the section on special problems of shallow water diving (p. 329).

The deep sea diving rig is composed essentially of a helmet and water-tight dress, weighted belt and shoes, a hose and control valve whereby air is furnished and the quantity of air controlled, and a nonreturn valve used to prevent air from escaping from the dress in the event of an accidental rupture of the air hose.

For an excellent description of deep sea diving equipment the reader is referred to a U. S. Navy publication (*3339*) 1951 which has now been incorporated into the Bureau of Ships Diving Manual, 1952, and can be obtained from the U. S. Government Printing Office, Washington 25, D. C. The section of the book devoted to diving equipment includes a description of the apparatus with pictures and cross-sectional diagrams. Additional information on this subject is supplied in a descriptive monograph by Davis (*3319* and *3330*) 1951.

Tests by Molumphy (*3336*) 1948 on the U. S. Navy deep sea diving helmet at depths of 0, 75, 150, and 225 feet, with supply pressures of 25, 50, 75, and 100 lbs. per square inch over bottom indicated that the ratio of total recirculation of high pressure-nozzle flow for helium-oxygen mixtures is about 7 to 1 and it was found to increase somewhat with depth. Practically no difference was found to exist in recirculation by the venturi system when the high-pressure nozzle was one-fourth inch away or flush with the mouth of the venturi discharge nozzle. All high-pressure nozzle and recirculation flows decreased with depth. For additional information on this subject the reader should avail himself of papers by Molumphy (*3335* and *3337*) 1948.

For other reports on diving procedures and equipment, the reader may consult papers by Delorme and Locke (*3331*) 1944; Klimenko, Pavlivskii, and Maksimenko (*3332, 3333,* and *3334*) 1948, and the U. S. Navy (*3338*) 1949.

3329. Davis, Robert H. A summary of the present state of the art of deep diving. pp. 1–25 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London. The Saint Catherine Press Ltd., 1951, 670 pp. [D]

3330. Davis, Robert H. The physics and physiology of deep diving. pp. 26–40 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London. The Saint Catherine Press Ltd., 1951, 670 pp. [D]

3331. Delorme, E. J. and W. Locke. Report in the medical aspects of diving practice of interest to the Royal Canadian Navy. Canada NRC. Proceedings of 3rd meeting of associate committee on naval medical research. *Project C4080,* 15 May 1944, 6 pp.

3332. Klimenko, N. A., K. A. Pavlovskii, and V. P. Maksimenko. The physics of diving. pp. 10–25 in: *Manual for divers of the navy.* Moskow, Military Printing office, 1948, 172 pp. (Russian text.)

3333. Klimenko, N. A., K. A. Pavlovskii, and V. P. Maksimenko. Safety rules for descent. pp. 64–78 in: *Manual for divers of the navy.* Moskow, Military Printing office, 1948, 172 pp. (Russian text.)

3334. Klimenko, N. A., K. A. Pavlovskii, and V. P. Maksimenko. Care and repair of diving equipment. pp.

127–135 in: *Manual for divers of the navy.* Moskow, Military Printing office, 1948, 172 pp. (Russian text.)

3335. Molumphy, C. G. Test of recirculation and jet flow of He–O_2 helmets from USS Thinga and USS Petrel. U. S. Navy. Naval gun factory, EDU. *Project no. SRD–235–46,* 11 March 1948, 7 pp.

3336. Molumphy, C. G. Test of total recirculation, jet flow and vacuum of a He–O_2 helmet submitted by the USS Kittiwake. U. S. Navy. Naval gun factory, EDU. 25 March 1948, 8 pp.

3337. Molumphy, C. G. Determination of total recirculation, vacuum, high pressure nozzle discharge and other general characteristics of the recirculating system of the standard U. S. Navy He–O_2 deep sea diving helmet under various conditions of depth and venturi supply pressures, with air and He–O_2 mixtures. U. S. Navy. Naval gun factory, EDU. *Project no. SRD 235/46,* 22 April 1948, 12 pp.

3338. U. S. Navy. BuNavPers. The descent. pp. 81–102 in: *Submarine medicine practice.* NavPers 10838, March 1949, 182 pp. [D]

3339. U. S. Navy. BuShips. Description and care of standard diving equipment. pp. 3–19 in: *Chapter 94. Salvage section II. Diving.* 25 January 1951. U. S. Government printing office, Washington, D. C., 1951, 93 pp.

VII. RESUSCITATION AND RESPIRATORY DEVICES

Aboard ships at sea during war many occasions are presented when life may be saved by prompt administration of artificial respiration. The main emergencies in which it is required are drowning and electric shock. Because the subject extends far beyond the scope of this volume, it has not been considered pertinent to include an extensive bibliography of the literature on artificial respiration or respiratory devices.

For general studies on artificial respiration, papers by the following authors should be consulted: André (*3340*) 1949; Behrens (*3343*) ; Davis (*3350*) 1947; Groesbeck (*3359*) 1951; Jellinek (*3362*) 1947 and (*3363*) 1951; Murray (*3372*) 1945; Whittenberger and Sarnoff (*3392*) 1950; Wiggin, Saunders, and Small (*3393* and *3394*) 1949; Wilson (*3395*) 1948; and U. S. National Research Council (*3397*) 1951. Reference 3398 may also be consulted.

In drowning and electric shock, respiratory failure occurs first and failure of the heart secondarily. When the activity of the medulla oblongata is depressed respiration becomes sluggish and may cease but the heart continues to beat independently of the central nervous system, provided it receives an adequate supply of oxygen. Therefore, if oxygen can be supplied to the patient's blood promptly the circulation will continue and the respiratory center may recover its rhythmic activity for natural and sustained respiration.

It is stated (*3393* and *3394*) that in the human being complete cerebral anoxia for 10 seconds produces unconsciousness, 20 to 30 seconds causes cessation of brain waves, and 3 to 5 minutes produces irreversible pathological changes in nervous tissue. Damage to the myocardium by anoxia is important because although it develops less rapidly than that to the brain, it is responsible for the inability of the heart to recover from cardiorespiratory arrest in cases in which cardiac resuscitation is unsuccessful. Wiggin, Saunders, and Small also state that if cardiorespiratory arrest has not lasted longer than 2 to 4 minutes, recovery may be expected. For another excellent review of resuscitation, the reader should consult the paper by André (*3340*) 1949. When cardiac massage is resorted to, this author favors the injection of one-half mg. of atropine as soon as the myocardial contractions have reappeared to avoid vagal inhibition when spontaneous respiratory movements reappear.

Conclusions drawn from the National Research Council conference on methods of artificial respiration (*3397*) indicate that the prone pressure method is unsatisfactory and should be abandoned. Because the arm-lift back-pressure method gives adequate ventilation and is easy to teach and can be carried out by a single operator for long periods of time, it was advised that this method be adopted for military use. The arm-lift chest-pressure method provides sufficient ventilation but is not conducive to a clear airway. Difficulty in teaching and learning the hip-roll back-pressure method was stated to be a deterrent to its acceptance and the hip-lift back-pressure method was stated to be too fatiguing for a single operator. This latter method gave the fullest pulmonary ventilation.

Experimental evidence presented by Gordon, Prec, Wedell, Sadove, Raymon, Nelson, and Ivy (*3355*) 1951 indicated no significant differences in the mean arterial oxygen saturation when hip-lift back-pressure, arm-lift back-pressure, hip-roll back-pressure and Eve methods were used. Fifteen normal male subjects (23 to 45 years old) were given curare to produce complete apnea. The right heart was catheterized via the external jugular or antecubital vein with the tip in the pulmonary artery one inch beyond the bifurcation. Another catheter was introduced into the right auricle and a third catheter was inserted in the femoral artery. High cardiac outputs of over 5.5 liters per minute were obtained for all methods. Great differences in pulmonary arterial pressures (inspiratory and expiratory) were found in all methods except for the Schaefer method. The mean level of arterial oxygen saturation for the Schaefer method was only 77 percent while for other methods it ranged between

89 and 100 percent. In the manual push-pull methods, a high carbon dioxide output and respiratory quotient indicated a high rate of enforced gas exchange. The Eve method gave uniform respiratory quotients with only small fluctuations.

Swann and Brucer (*3386*) 1948 found in dogs that the first sign of recovery during resuscitation was a sharp rise in systolic pressure but not necessarily a rise in diastolic pressure. Soon thereafter breathing was reinstated. Animals were given air mixtures of 2.4 percent oxygen in nitrogen and when death was imminent, various lung ventilation measures were instituted to resuscitate the animals. The first rise in blood pressure occurred within 100 seconds or not at all, even though pulmonary ventilation was continued for 20 minutes. When cardiac massage, as well as artificial respiration, was instituted, recovery was facilitated. However, return of blood pressure and respiration was slower.

For additional papers of cardiovascular responses occurring during resuscitation, the reader should consult reports by Binet and Strumza (*3345*) 1951; Fainer, Martin, and Ivy (*3352*) 1951; Handford, Ricchiuti, and Bodenlos (*3360*) 1951; Lapin (*3370*) 1945; and Wilson (*3396*) 1949.

Respiratory studies by Asmussen and Nielsen (*3341*) 1950 on 6 male and 5 female subjects given artificial respiration by the Schaefer, Nielsen and Eve methods gave tidal air values of 180 cu. cm. for the Schaefer method, 450 cu. cm. for the Nielsen, and 540 cu. cm. for the Eve method. Two patients with respiratory arrest were subjected to different methods of artificial respiration by Comroe and Dripps (*3349*) 1946. The tidal air from the Schaefer method varied from 71.5 to 117 cu. cm. while the Eve method produced exchanges ranging from 286 to 500 cu. cm. per cycle. Because the Schaefer method depends primarily on the elastic recoil of the lungs and tone of the respiratory muscles and since these are absent in the deeply asphyxiated patient, this method is of least value when needed most. Conversely, the Eve method is efficient when tone and elasticity of these structures is absent. It was also found that intratracheal insufflation with oxygen is not as effective as actual expansion and collapse of the lungs for the movement of carbon dioxide from the alveolar surfaces. This is explained by the fact that carbon dioxide has a greater molecular weight than oxygen and does not diffuse as rapidly as oxygen, despite the greater ease with which it diffuses through water and living membranes. The accumulation of lactic acid due to severe tissue anoxia and fixed retention resulting from intense renal vasoconstriction caused by too low blood pressure were probably responsible for some of the acidosis that developed. These studies by Comroe and Dripps emphasize that artificial respiration must not only raise blood oxygen levels to normal levels but must also reduce the blood carbon dioxide.

Additional papers by Gordon, Affeldt, Sadove, Raymon, Whittenberger, and Ivy (*3354*) 1951; Nims, Conner, Botelho, and Comroe (*3373*) 1951; Thompson (*3387*) 1948; and Whittenberger, Affeldt, Goodale, and Sarnoff (*3391*) 1951 indicate that tidal air volumes for the Schaefer method are considerably lower than those obtained by the other methods of manual artificial respiration. These other push-pull methods have been found to be at least 2 times more efficient for pulmonary ventilation than the Schaefer method. Pneumotachographic studies dictate that active inspiration and active expiration should ideally occupy approximately one and a half second each. Best performance was obtained by a 5 to 6 second cycle with 10 to 12 cycles per minute. Although the Nielsen method produced less pulmonary ventilation than the hip-lifting procedures, it appeared to be a convenient and practical method for giving artificial respiration for long periods of time. It is recommended (*3373*) that since the blood carbon dioxide level has risen in the apneic patient, a breathing frequency in excess of 10 to 12 per minute should be used.

Further studies on respiratory effects of resuscitation have been reported by Carson and Pinto (*3348*) 1947; De Forest and Potthoff (*3351*) 1951; Gordon, Sadove, Raymon, and Ivy (*3357*) 1951; Karpovich, Hale, and Bailey (*3367*) 1951; Pask (*3374*) 1948; Sadove, Gordon, Nelson, and Ivy (*3377*) 1951; Spiro, Aaron, and Thompson (*3382*) 1947; Spiro, Goltra, and Thompson (*3383*) 1948; and Swann (*3384*) 1948 and (*3385*) 1949.

Karpovich and Hale (*3365*) 1951 measured the energy expenditure of 20 men and women performing 5 methods of artificial respiration. Oxygen consumption for the methods was as follows: Schaefer, 547 cu. cm. for men and 445 cu. cm. for women; Silvester, 706 cu. cm. and 480 cu. cm.; Nielsen, 706 cu. cm. and 657 cu. cm.; hip-roll back-pressure, 1,045 cu. cm. and 746 cu. cm.; and the hip-lift back-pressure, 1,050 cu. cm. and 713 cu. cm. Work by Gordon, Raymon, Sadove, Wedell, and Ivy (*3356*) 1951 leads them to conclude that the Schaefer method is least taxing; the hip-lift back-pressure requires the greatest energy expenditure while the Silvester and Nielsen methods are intermediary.

The ease of teaching the various methods of manual artificial respiration was investigated by Karpovich and Hale (*3364*) 1941 and (*3366*) 1951. One hundred academy cadets and 67 college students were instructed in 5 methods of artificial respiration. From the standpoint of ease of learning and operation, these methods have been arranged in the following order of increasing difficulty: prone pressure, arm-lift back-pressure, arm-lift chest-pressure, hip-roll back-pressure, and hip-lift back-pressure. Gordon, Star, Meier, Hale, and Ivy (*3358*) 1951 found that the arm-lift back-pressure and variations of the hip-lift back-pressure methods could be successfully taught to naval recruits, including Waves, in relatively brief training sessions. Of these methods, the arm-lift back-pressure surpasses all the variations of the hip method in accuracy of performance, ease of learning, and physical ease of performance.

For additional papers on artificial respiration the reader should consult papers by Baetjer (*3342*) 1951; Brucer and Swann (*3346*) 1951; and Schwerma, Ivy, Friedman, and La Brosse (*3380*) 1948.

It is not intended under this heading to include in its entirety the extensive literature on resuscitative equipment. A paper by Schwerma and Ivy (*3379*) 1946 contains information on pathological damage of lungs resulting from excessive positive and negative pressures of respirators in dog experiments. The reader should also consult reports such as those by Campbell and Poulton (*3347*) 1938 and Fisher (*3353*) 1950 for discussions and descriptions of respiratory devices now in use.

3340. André, M. J. La ranimation en chirurgie traitement physiologique de la syncope (A l'exclusion de l'oxygéno-carbothérapie). *Anest. & Analges., Paris,* 1946–49, *6:* 128–165. [R]

3341. Asmussen, E. and M. Nielsen. Efficacy of artificial respiration. *J. appl. Physiol.,* 1950, *3:* 95–102.

3342. Baetjer, A. M. Resuscitation. pp. 1022–1027 in: *Rosenau preventive medicine and hygiene.* Edited by Kenneth F. Maxcy. Seventh edition. New York, Appleton-Century Crofts, Inc., 1951, 1462 pp. [R]

3343. Behrens, C. F. Asphyxia in naval operations. U. S. Navy. NMRI. Lecture and review series. *No. 51–8.* 12 June 1951, 7 pp.

3344. Berger, L. B. Supplemental list of respiratory protective devices approved by the Bureau of Mines. Additions to list published in Information Circular 7444. U. S. Bureau of Mines. *Information Circular 7513.* April 1949, 3 pp.

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3346. Brucer, M. and H. G. Swann. Requirements for resuscitation by artificial respiration in fulminating anoxia. *J. appl. Physiol.,* 1951, *3:* 479–488.

3347. Campbell, A. and E. P. Poulton. Artificial respiration. pp. 147–150 in: *Oxygen and carbon dioxide therapy.* London, Oxford University Press, 1938, 202 pp.

3348. Carson, L. D. and J. C. Pinte. The Eve method of resuscitation. *Nav. Med. Bull., Wash.,* 1947, *47:* 650–656. *J. industr. Hyg.,* 1948, *30:* abstract section: 3. [P] [R]

3349. Comroe, Jr., J. H. and R. D. Dripps. Artificial respiration. *J. Amer. med. Ass.,* 1946, *130:* 381–383. *J. industr. Hyg.,* 1946, *28:* abstract section: 71–72. [R] [CH]

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3352. Fainer, D. C., C. G. Martin, and A. C. Ivy. Resuscitation of dogs from fresh water drowning. *J. appl.* Physiol., 1951, *3:* 417–426. [P]

3353. Fisher, H. E. Resuscitation. pp. 876–878 in: *Medical physics. Volume II.* Edited by Otto Glasser. Chicago, The Year Book Publishers, Inc., 1950, 1227 pp. [R]

3354. Gordon, A. S., J. E. Affeldt, M. Sadove, F. Raymon, J. L. Whittenberger, and A. C. Ivy. Air-flow patterns and pulmonary ventilation during manual artificial respiration on apneic normal adults. *J. appl. Physiol.,* 1951, *4:* 408–420. [P]

3355. Gordon, A. S., O. Prec, H. Wedell, M. S. Sadove, F. Raymon, J. T. Nelson, and A. C. Ivy. Circulatory studies during artificial respiration on apneic normal adults. III. *J. appl. Physiol.,* 1951, *4:* 421–438. [P]

3356. Gordon, A. S., F. Raymon, M. S. Sadove, H. Wedell, and A. C. Ivy. Energy expenditure of operators during manual artificial respiration. IV. *J. appl. Physiol.,* 1951, *4:* 439–446. [P]

3357. Gordon, A. S., M. S. Sadove, F. Raymon, and A. C. Ivy. Critical survey of manual artificial respiration. *J. Amer. med. Ass.,* 1951, *147:* 1444–1453. [R]

3358. Gordon, A. S., S. Star, F. Meier, C. Hale, and A. C. Ivy. Pedagogical and performance factors of manual artificial respiration with naval personnel. *V. J. appl. Physiol.,* 1951, *4:* 447–457. [P]

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3365. Karpovich, P. F. and C. J. Hale. Energy expended in administering artificial respiration. *J. appl. Physiol.,* 1951, *4:* 467–471. [P]

3366. Karpovich, P. V. and C. J. Hale. Manual artificial respiration. Pedagogical and fatigue factors involved in its use. *J. appl. Physiol.,* 1951, *4:* 472–475. [P]

3367. Karpovich, P. V., C. J. Hale, and T. L. Bailey. Pulmonary ventilation in manual artificial respiration. *J. appl. Physiol.*, 1951, *4:* 458–466. [P]

3368. King, B. G., E. P. Vollmer, D. E. Goldman, and J. B. Dorner. Evaluation of the Heidbrink model–70 and army item no. 37261 positive pressure resuscitators and Kreiselman hand bellows resuscitator with field tests in collaboration with Naval Air Station, Lakehurst, New Jersey. U. S. Navy. NMRI. *Project X–486, Rept. no. 2,* 7 May 1945, 13 pp.

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3373. Nims, R. G., E. H. Conner, S. Y. Bothelho, and J. H. Comroe, Jr. Comparison of methods for performing manual artificial respiration on apneic patients. *J. appl. Physiol.*, 1951, *4:* 486–495. [P]

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3388. Vollmer, E. P. Appraisal of two resuscitation devices made up of obsolete oxygen equipment. U. S. Navy. NMRI. *Project X–486, Rept. no. 4,* 25 June 1945, 3 pp.

3389. Vollmer, E. P., B. G. King, and J. A. Peck. Evaluation of the Burns pneumatic balance resuscitator. U. S. Navy. NMRI. *Project X–486, Rept. no. 5,* 2 July 1945, 6 pp.

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3394. Wiggin, S. C., P. Saunders, and G. A. Small. Resuscitation (concluded). *New Engl. J. Med.*, 1949, *241:* 413–420.

3395. Wilson, J. W. Studies in resuscitation. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. MCREXD–696–79G,* 28 April 1948, 128 pp. [P]

3396. Wilson, J. W. Studies in resuscitation by Dr. H. G. Swann. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. MCREXD–696–79G,* 28 March 1949, 89 pp. [P]

3397. U. S. NRC. Division of Medical Sciences. Ad hoc conference on manual methods of artificial respirations. Minutes of first meeting, 1 October 1951, 16 pp.

3398. Anon. Artificial respiration: Its importance to you. *Clin. Med.*, 1945, *52:* 192–194.

VIII. DIFFUSION RESPIRATION

It is not intended under this heading to make any attempt to include in its entirety the literature relating to diffusion respiration. The selected references on diffusion respiration which follow are discussed here because from this literature are to be derived data which can be applied to respiratory problems of divers and underwater swimmers.

Alveolar carbon dioxide levels of dogs subjected to 45 minutes of apnea after oxygen inhalation were measured by Roth, Whitehead, and Draper (*3404*)

1947. Following denitrogenation, breathing was arrested by continuous infusion anesthesia. After collection of air samples, the animals were revived by artificial respiration. After 30 minues of diffusion respiration the alveolar carbon dioxide concentration had risen to 13.3 percent and after 45 minutes had risen to 43.0 percent. In the 4 dogs exposed to room air 3 minutes after their removal from the oxygen chamber, the alveolar carbon dioxide concentration had fallen to 9.9 percent.

Similar work by Binet and Strumza (*3399*) 1947 on 15 dogs showed plasma carbon dioxide levels of 55.8 volumes percent after 20 minutes, 73.7 after 60 minutes, and 88.9 volumes percent after 2 hours. The hypercapnia was associated with a lowering of pH, a value of 6.8 being manifested after 2 hours. Blood pH levels of 6.78 after 45 minutes of apnea were reported by Draper, Whitehead, and Spencer (*3401*) 1947. An hour after institution of artificial respiration the pH of the venous blood had risen to 7.32. Of 12 dogs subjected to apnea after oxygen inhalation, one died 96 hours after resuscitation. The authors attribute the survival and ultimate recovery of these dogs to the suction inward of respiratory gases to the hemoglobin-oxygen "pump".

Dogs subjected to diffusion respiration for two 45-minute period demonstrated an initial fall of systolic pressure, but thereafter this was well maintained during the remaining period of respiratory arrest. Parry, Spencer, Whitehead, and Draper (*3403*) 1948 also reported ventricular extrasystoles during the first phase of diffusion respiration which disappeared during the latter phase of apnea. These authors (*3405*) 1948 also reported that in dogs given thiopental after denitrogenation, the oxygen uptake decreased approximately 11 percent. Similar values were obtained with curare. This level was maintained for 30 minutes, then gradually fell to reach a level 30 percent less than the control value. The maximum negative intrapulmonary pressure developed in this series of experiments exceeded 10 cm. of water.

For other articles concerned with diffusion respiration, the reader is recommended to consult reports by the following authors: Draper and Whitehead (*3400*) 1951 and Ferris (*3402*) 1951.

3399. Binet, L. and M. V. Strumza. Vie en apnée dans un milieu d'oxygène pur. *C. R. Acad. Sci., Paris,* 1947, *225:* 12–14.

3400. Draper, W. B. and R. W. Whitehead. The phenomenon of diffusion respiration. *Curr. Res. Anesth.,* 1949, *28:* 307–318. *Excerpta Medica,* (Section II. Physiology, Bio-chemistry and Pharmacology), 1951, *4:* 302. Abstr.

3401. Draper, W. B., R. W. Whitehead, and J. N. Spencer. Studies on diffusion respiration. III. Alveolar gases and venous blood pH of dogs during diffusion respiration. *Anesthesiol.,* 1947, *8:* 524–533. [P]

3402. Ferris, B. G., Jr. Problems of diffusion in the lungs. *Bull. New Engl. med. Center.,* 1950, *12:* 144–153. *Excerpta Medica.* (Section II. Physiology, Biochemistry and Pharmacology), 1951, *4:* 646, Abstr.

3403. Parry, T. M., J. N. Spencer, R. W. Whitehead, and W. B. Draper. Changes in heart rate, blood pressure and electrocardiogram in dogs during diffusion respiration. *Amer. J. Physiol.,* 1948, *155:* 459. Abstr.

3404. Roth, L. W., R. W. Whitehead, and W. B. Draper. Studies on diffusion respiration. II. Survival of the dog following a prolonged period of respiratory arrest. *Anesthesiol.,* 1947, *8:* 294–302. [P]

3405. Spencer, J. N., W. B. Draper, T. M. Parry, and R. W. Whitehead. Studies on diffusion respiration. v. The hemoglobin-oxygen pump. *Fed. Proc. Amer. Soc. exp. Biol.,* 1948, *7:* 119.

IX. PRESSURE BREATHING

Aside from therapeutic applications of pressure breathing, information arrived at from research in this respiratory field is also applicable to the design and development of underwater swimming gear for shallow water swimmers. Impetus was given to this field by military research during World War II, the primary purpose being to increase the ceiling of aviators at very high altitudes by raising the partial pressure of oxygen in the lungs. Many modifications of pressure breathing equipment have been developed for delivering gases under pressure to the lungs, giving almost every conceivable pattern of pressure breathing.

In 1947, Barach, Fenn, Ferris, and Schmidt (*3409*) reviewed the literature on the physiology of pressure breathing. It is stated that pressure breathing will not lead to serious difficulties provided the pressures within the mask do not exceed 15 mm. of Hg. The difficulty of expiring against a continuous pressure can be avoided by the use of intermittent pressure breathing devices which keep the pressure high on inspiration and low on expiration. This usually results in hyperventilation and will probably lead to decreased performance if the alveolar carbon dioxide tension falls below 25 mm. of Hg.

Decreases of function produced by exposures to 47,000 feet in men breathing with a continuous positive pressure of 15 mm. of Hg. have been reported by Barach, Eckman, Bloom, Eckman, Rule, Rumsey, and Wortis (*3406*) 1947. Exposures to 42,000 feet with a continuous positive pressure of 15 mm. Hg. produced no measurable decrease in performance. All subjects complained of a post-flight fatigue which became progressively worse as the number of exposures was increased. The occurrence of two cases of syncope and three of imminent collapse in 17 subjects breathing with a positive pressure of 15 mm. Hg. during flights at 44,800

feet while runs to 42,000 feet resulted in no syncope or collapse indicated that the stability of the individual may be impaired by pressure breathing at this critical altitude.

Regarding the effect of increased positive intrapulmonary pressure on the muscular response, Bean and Elwell (*3412*) 1950 found that there was an augmentation of tibialis anticus contractions elicited by slow single shock motor nerve stimulation. This has been ascribed to an influence on the myoneural junction induced by the alteration in blood flow which results from positive intrapulmonary pressure. The finding that augmentation occurred in direct stimulation of the normal muscle, but was missing in such stimulation of the chronically denervated muscle supports this interpretation.

According to De Lalle (*3418*) 1948 the reduction in skin temperature of men using pressure breathing apparatus is the result of peripheral vasoconstriction. In his studies, subjects wore the U. S. Air Force A–13 mask connected to a pump and tank giving intermittent pressures ranging between -20 to $+20$ cm. of water. These pressures were administered for 10 minutes. Navy pneumatic vests were also worn by the eleven subjects. All subjects experienced a $-0.3°$ C. fall of finger skin temperature being reduced somewhat after 7 minutes of pressure breathing. The inflated vests seemed to increase the magnitude of skin cooling. This vasoconstrictor response did not depend on expansion of the chest because it occurred in negative pressure breathing or when expansion of the chest was prevented by expansion of the pneumatic vest. Bateman and Sheard (*3410 and 3411*) 1946 also reported a slight decrease in skin temperature during pressure breathing but this fall was followed by a slow rise which as a rule exceeded the initial decrease so that the peripheral vessels became more dilated than they were in the control period at ambient pressure.

Experimentally, Werkö (*3440*) 1947 found that intermittent pressure breathing produced small blood pressure changes in persons with normal circulatory systems and variable changes in patients with cardiovascular disease. When a mixture of 10 percent oxygen in nitrogen was used, the pulmonary arterial pressure was increased and was accompanied by an increase in pulmonary vascular resistance. In one case with normal circulation using a continuous pressure breathing device, there was a reduction in cardiac output corresponding to a low mean mask pressure accompanied by increases in arterial, right ventricular and pulmonary arterial pressures. The automaticity of the intermittent pressure devices reduces labored breathing. When the mean mask pressure and consequently the rise in pleural pressure is small, no decreases in cardiac output should occur. The author states that when intermittent pressure equipment is used for artificial respiration, the inspiratory period with a high pressure should be short and the expiratory period long. Expiratory mean mask pressure should be as near atmospheric pressure as possible so as not to produce any added adverse effects on the circulation.

According to Cournand, Motley, Werkö, and Richards (*3417*) 1948, cardiac output is decreased in proportion to the increase in mean mask pressure when respirators are used having expiratory times equivalent to inspiratory periods with expiratory pressures above atmospheric. Decreased cardiac output is also produced when the inspiratory pressure is rapidly increased and then dropped rapidly during expiration, the latter pressure being above atmospheric. The net filling pressure of the right ventricle was decreased during the phase of increased mask pressure and increased during the phase of decreasing mask pressure. Conversely, when cardiac output was increased, the mean net filling pressure was increased. The authors interpreted these changes as being suggestive of a deficit in cardiac output during the inspiratory phase, compensated for in the expiratory phase. When the pressure drop is rapid in expiration with a resulting low intrapleural pressure, compensation is complete, provided the expiratory period is of sufficient duration. Expiratory time must equal or exceed inspiratory time in order that the number of heart beats during expiration may equal or exceed the number present during inspiration. It was recommended that intermittent positive pressure breathing apparatus should allow for a gradual increase in pressure during inspiration, a rapid drop in pressure after cycling, a mean mask pressure practically equivalent to atmospheric pressure during expiration, and an expiratory time equal to or greater than the inspiratory phase.

Studies by Fenn and associates (*3422* and *3423*) 1947 demonstrated, with a newly designed finger plethysmograph, a decrease in finger volume when men respired with a positive pressure respirator. A pressure of 30 cm. of water was applied to the lungs through the medium of a pressurized helmet. It was felt that this decrease in blow-flow due to positive pressure breathing was chiefly the result of a vasoconstriction and only to a small extent due to an increase in venous pressure. Volume measurements of the legs during positive pressure breathing showed an increase in volume, as measured by a boot plethysmograph. This is believed to be due to a passive inflation of the veins.

Information concerning fluid shifts in men using positive pressure breathing respirators can be obtained from papers by Henry (*3426*) 1951; Henry, Hendrickson, Movitt, and Meehan (*3427*) 1948; Henry, Jacobs, Meeham, and Karstens (*3428*) 1948; and Jacobs, Karstens, and Henry (*3433*) 1948. According to Henry (*3426*), when man breathes against pressures as high as 60 mm. of Hg., the available blood reserve is lost into the limbs in two ways: (1) by venous distention and (2) by cutting down the blood volume through fluid filtration caused by high pressures in minute vessels, the loss being greater in a warm environment. Because the blood volume is inadequate, diastolic filling of the heart is impaired and may decrease to a point where ventricular emptying will be completed before the systolic phase has been terminated. This results in an abnormal squeezing and rubbing of the empty ventricular walls which may result in afferent firing of the vagus to initiate reflex peripheral vasodilatation and collapse characteristic of vasovagal syncope. The author concludes from this that pressure suits should be used in ascending from the 40,000 foot level to prevent the loss of blood into the limbs.

Henry, Jacobs, Meeham, and Karstens (*3428* and *3433*) 1948 reported an increase in mean venous pressure during pressure breathing when the intrathoracic pressure had reached levels of 20 to 60 mm. Hg. Hematocrit and hemoglobin measurements on 8 subjects indicated a hemoconcentration which increased in proportion to the pressure used. At 30 mm. Hg. mean intrathoracic pressure the fluid loss in 30 minutes was 4.0 ± 0.5 cu. cm. per 100 cu. cm. of blood. Aside from fluid losses during pressure breathing, an increase in venous pressure occurred in those vessels lying outside of the raised pressure areas of the head and trunk. The distention of these vessels aided the pooling of blood outside of the pressure areas. Determinations of volume changes were made by measuring the differences in volume of the blood in both legs and one arm isolated by arterial occlusion cuffs. The estimated volume decrease of 300 cu. cm. of 6 percent of total volume was in fair agreement with estimations made with plethysmographic and teeter-board methods. When pressures above 40 mm. Hg. were used, the fluid losses were greater. These changes are in themselves adequate to account for the frequent development of syncope during periods of raised intrathoracic pressure.

An experimental study was conducted by Cain, Wood, and Mahoney (*3415*) 1950 to determine the time tolerance of a group of individuals breathing at various positive pressures from 30 to 60 mm. Hg. at room temperatures of 65° and 95° F. A fairly narrow time range of tolerance occurred with the high pressures of 50 and 60 mm. Hg. This range widened considerably at 30 and 40 mm. Hg., approximating time tolerance of 1 minute at 60, 7 minutes at 50, and 15 minutes at 40 mm. Hg. When breathing against 30 mm. Hg., the time was extended to 1 to 2 hours and the exposures were terminated because of fatigue, rather than impending syncope.

Subjects exposed to 40,000 feet using positive pressure breathing equipment developing a mask pressure of 15 mm. Hg. had an increase in arterial oxygen saturation equivalent to that obtained by a 15 mm. Hg. increase in barometric pressure. Barach, Eckman, Eckman, Ginsburg, and Rumsey (*3407*) 1947 stated that their data gave no indications which would suggest a change in the operation of the laws concerned with the transfer of gas from the lungs to the blood at very high altitudes.

For an authoritative review of the respiratory effects of positive pressure breathing, the reader is referred to the article by Wyss (*3443*) 1949. The capacity and resistance of the pulmonary vascular bed and the effects of airway pressure on the alteration of fluid exchange in the lungs during intermittent positive pressure breathing have been investigated by Maloney and Whittenberger (*3436*) 1951. In a series of dog experiments, measurements of intrapleural pressure, alveolar pressure, and pulmonary "capillary" pressure were made. From the data collected it became apparent that two factors of major importance were: (1) the effects of alteration of venous return brought about by changes of pressure relationships in the venous system within and without the thorax, and (2) the effects of lung volume change. At a given lung volume it was found that intrapleural pressure, alveolar pressure, and pulmonary "capillary" pressure bore the same relationship to each other, regardless of the method used to inflate the lungs. It was concluded that the hemodynamic effects of pressure breathing were due to effects on venous return, and not to any direct effect on the lungs other than volume change.

According to Barach, Eckman, Ginsburg, Rumsey, Korr, Eckman, and Besson (*3408*) 1946, breathing under a positive pressure of 15 mm. Hg. with a demand pressure regulator resulted in increase of functional residual air and frequently elevation of minute and tidal volumes. These changes were reduced when a vest or vest-pants apparatus was used, the pressure applied being equal to that of the mask. The effects resulting from

added resistance to respiration were investigated by Cain and Otis (*3414*) 1949. In resting subjects breathing through a "Y" tube, to which was connected a flow meter, resistance disc, and strain gage, the inspiratory and expiratory work required to overcome breathing resistance was measured. The average efficiency for the extra work of a complete respiratory cycle on a resistance of 0.385 mm. water per cu. cm. per second was 33 percent. The expiratory reserve increased 275 cu. cm. This change in expiratory reserve favors the muscles of expiration. It was found that breathing against a resistance decreases the total ventilation and brings about an increase of alveolar pCO_2 and a decrease in pO_2. Ballistocardiograms showed an increase in cardiac minute volume during inspiration and a decrease during expiration against a resistance of 0.385 mm. Hg. per cu. cm. per second. Cardiac minute volume was decreased 4 percent. Ivy, Adler, Snapp, and Bancroft (*3432*) 1949 subjected nembutalized dogs to respiration pressures ranging from 4 to 29 cm. of water and measured changes in intracranial pressure. When the intracranial pressure was at a level of 25 to 50 cm., pressure breathing caused an infrequent rise of 10 cm. in the intracranial pressure. A fall in intracranial pressure of the order of 15 cm. was observed during pressure breathing when the intracranial pressure was at a level of 60 to 80 cm. of cerebrospinal fluid.

In studies on kidney function in men exposed to 30-minute periods of continuous pressure breathing at 10, 20, 30, and 40 mm. Hg. above ambient pressure, Drury, Henry, Goodman (*3420*) 1947 found a progressive reduction of kidney function which, with the higher pressures, reached approximately 20 to 50 percent of normal values. This depression in function persisted for 1 or 2 hours after the cessation of pressure breathing. The authors believe that these results support the view that estimations of kidney function may be used as a measure of the circulatory stress induced by a reduction of effective blood volume.

Hyman and North (*3431*) 1941–1946 decompressed men to 35,000 feet using pressure breathing equipment operating at pressures of 6 and 8 in. of water. No great effect on the frequency of occurrence of decompression sickness was found when compared with the occurrence of these symptoms in the same subjects decompressed with normal oxygen supply equipment. Hardy and Barach (*3425*) 1945 describe the beneficial use of positive pressure respiration in the therapy of an 11-year-old boy having pulmonary edema incurred by inhalation of chlorine gas. Prompt improvement was noted when a pressure of 4 cm. of water was imposed during expiration. This patient had inhaled in a single inspiration some freshly prepared chlorine. Painful, persistent coughing ensued for 2 hours. Some relief was given by one-half grain of codeine. One hour later the cough returned with labored, rapid breathing, exhaustion, vomiting, and a fast, thin pulse. Loud rhonchi were heard throughout the chest bilaterally. The patient was placed in an oxygen tent containing 40-percent oxygen. After 4 hours in the tent, fine moist rales were present in the left lower lobe laterally and at the left border of the heart. Fifteen hours later the pulse was feeble, irregular and cyanosis was recognizable. A mask was applied delivering 50-percent oxygen at 4 cm. pressure. The following day most of the moist sounds had disappeared. A normal pulse did not return for 3 days.

For further studies on pressure breathing, reference may be made to papers by Bickerman and Beck (*3413*) 1950; Carr and Essex (*3416*) 1946; Drinker (*3419*) 1945; Fenn (*3421*) 1950; Gillick and Schneider (*3424*) 1949; Hyman and Goodman (*3429*) 1948; Hyman and Klain (*3430*) 1946; Kaufman, Nims, Nyboer, and Somberg (*3434*) 1944; Maloney (*3435*) 1950; Otis, Suskind, and Rahn (*3437*) 1948; Ryder and Kehoe (*3438*) 1948; Tatum and Himmelfarb (*3439*) 1945; Whittenberger (*3441*) 1950; and Wilson (*3442*) 1946.

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Selection and Training of Submarine Personnel, Divers, and Compressed Air Workers

I. SELECTION

For general discussions of the subject of selection of submarine personnel in the U. S. Navy, the following references should be consulted: *3457, 3464, 3485* and *3495*. Cronbach (*3457*) 1949 has indicated that selection research has increased the effectiveness of military forces by placing superior men in responsible posts. Selection and placement of men can be improved by mathematical studies of mass processing, the multiple cut-off method, and factor analysis. Billets should be studied in terms of human requirements and the significant human aptitudes should be classified. Test design should be deliberate, based on principles of measurement rather than a trial and error process. Basic studies of test design are considered by the author to be much needed. Improved technical methods of classifying men must be supplemented by careful use of the methods. A frontier barely explored is personality assessment. The author stresses that tests of personality can be improved. Future studies should consider how normal men function rather than identify potential break-down cases only. Research, according to the author, has been handicapped by inadequate criteria of proficiency. Procedures for judging effectiveness of men on the job should be further developed. Herrick (*3464*) 1951 has pointed out that the selection system at first was a negative one, involving the weeding out of those men who might be potentially dangerous due to marked deficiencies of hearing, speech or motor-coordination. In general (*3485*) the submariner is considered to be an individual who is average or above average in mental capacity and education, who is strong and in good health, who is well adjusted emotionally and temperamentally to himself and to his fellow men, and desires submarine duty. A selection screening program involves the elimination of personnel below median intelligence and the maintenance of rigorous standards of physical requirements—particularly with reference to special senses—and freedom from chronic disease. It is agreed that only those men should be accepted for submarine service who are highly motivated. This involves, however, an evaluation of the basis for motivation, the quality of motivation, and the sustained character of motivation.

Willmon (*3495*) 1948 has stated that selection of officers and men for submarines resolves itself into a process of determining the adequacy of the individual as regards intelligence and education, physique and health, emotionality and personality. Attrition is seen to be due for the most part to inadequate scores in classification tests, over-age, and defective vision. As Willmon has emphasized, there is no place in submarines for the emotionally immature, the emotionally unstable, the neurotics, or psychopaths. Only one serious mistake is made in the life of a submarine. Clues to personality disturbances may be given by a bad civilian or military record, a history of repeated shifting of jobs for no real reason, repeated discharges from employment, multiple divorces, or repeated family difficulties. A history of nail-biting, constipation, frequently upset stomach, diarrhea, frequent headache, somnambulism, somniloquism, tachycardia, hypertension, and wet palms may all serve to identify the temperamentally ill-adapted candidate. Four of the following traits are suggested as placing a candidate in a doubtful category and 6 or more are offered as predicting probable break-down under stress: (1) bed-wetting beyond the age of 4 years; (2) thumb-sucking or nail-biting beyond 6 years; (3) failure to engage in competitive games involving risk of

injury; (4) tantrums in childhood; (5) abnormal shyness or sensitiveness; (6) preference for playing alone; (7) repeating grades in school, chronic truancy or difficulty with teachers; (8) abnormal fears; (9) shunning girls after puberty; (10) fainting; (11) excessive autonomic system reactions to emotion (tremor, abnormal sweating, tachycardia, etc.); (12) sulkiness under discipline; (13) abnormal attachment to mother after puberty; (14) stammering; (15) obsessional traits.

In a paper on the development of selection procedures, Shilling and Kohl (*3482*) 1945 have pointed out that at the onset of the war, the physical examination was the only examination for entry into submarine duty. Some requirements were unrealistic and underwent modification. Selection of sonar operators brought about new testing procedures. Psychological testing came into the picture with various paper and pencil tests and other methods. In 1943 a trained psychiatrist was used at New London in selection, interviewing those candidates who failed the paper and pencil tests. Submarine crews returning from combat were reexamined with the result that many were eliminated who should never have been assigned to submarine duty in the first place. In 1943 an interview board traveled to officer indoctrination units to interview aspirants for submarine training. These same board members served on a final review board for all officer candidates. Checking their findings with final accomplishments of personnel indicated a high proficiency of selection procedures. The escape training tank was used not only for escape training directly but also in providing stressful situations in which emotional adaptability could be evaluated. Two U. S. Navy reports published in 1946 (*3486* and *3487*) may be consulted for comments on submarine personnel classification. These reports stressed the following defects of wartime classification: (1) undue complexity, (2) misplaced emphasis, and (3) inadequate indoctrination of forces afloat in use of classification data. Various suggestions on methods of classification were set forth.

In 1944 Willmon and Bartlett (*3496*) reported a standard form that would provide some indication of the performance of every graduate of the submarine school. Previously, general information on performance of men at sea had been obtained informally from the commanding officers. It was anticipated that the new procedure would afford detailed information to guide selection. An accounting method was established to trace every candidate reporting for examination for submarine school until either he left the submarine service or completed one patrol on a submarine. Data on each of the steps in processing a man were referred to a common information center where machine accounting facilities were available. An early study of the data collected in this manner pertained to the problem of age or maturity of submariners and led to the conclusion that it might be advisable to set the lower age limit at 19, thus eliminating the 17- and 18-year old groups.

Bartlett (*3445*) 1945 also contended that, other factors being equal, older men are preferred to young men of 17 and 18 years of age. In a correlation of tests with grades in submarine school, Bartlett found that a combination of scores for the general classification test, the arithmetic reasoning test, and the mechanical knowledge test, is a better index of grades in submarine school than is the general classification test score alone. From statistical data presented in an earlier report in 1942 (*3488*) it was apparent that sole reliance could not be placed on the general classification test for selection of personnel. It was also apparent at that time that some more comprehensive study would have to be completed to determine a more reliable standard than had been presented by any of the reports to that date. Bartlett (*3445*) concluded that the population of the submarine schools could be improved with respect to training performance by further selection on the basis of test scores. The ages of students were found to be related to grades in submarine school, but the degree of relationship did not seem to warrant any change in the then present age standard in order to improve training performance. Similarly no change in standards for educational level seemed indicated.

In 1945 Bartlett (*3447*) made an evaluation of the officer classification test as a device for selecting officer candidates for submarine school. He reported that officer classification test scores were correlated significantly with performance in submarine school. A score combining sections of the test was found to be the most significant index of subsequent academic standing, but if any single section score had to be employed the mathematical score was probably the most satisfactory of the different scores. Candidates with previous submarine indoctrination achieved higher standings than did those without indoctrination. The class standings of officers with previous indoctrination could be predicted with more confidence from the aptitude scores than could the standings of officers without indoctrination. In 1946 Bartlett (*3449*) carried out an investigation of the billet qualifications blank (NavPers 16418) to test its suitability with combat-

experienced candidates for submarine training. His studies warranted the assumption that personality tests could be utilized to good effect with a combat-experienced population. In 1946 Bartlett presented two reports (*3450* and *3451*) describing an abstract of the service record for analysis of examinations of experienced submarine personnel received for reassignment. This record was developed to allow a systematic accounting of examinations of experienced submarine personnel received at the U. S. Submarine Base, New London, Conn., for reassignment. The record was designed to list men examined for reassignment by rate, age, and by experience and to analyze reasons for failure in medical examinations. The record also made it possible to tabulate failures in examinations for specialties, such as sonar, radar, and night vision, and to allow analysis of such failures by rate, age, and collateral test scores. The record also made it possible to maintain psychological quality control data on men examined and to accumulate gradually a master file of enlisted submarine personnel with pertinent experience data from their service record.

From the date of the entrance of the United States into World War II to the middle of 1945 a total of 33,011 enlisted men were received for training in the submarine service of the U. S. Navy. Of this number, 6,040 were disqualified by the examiners. A total of 24,752 men were enrolled in the submarine school where 771, or approximately 3 percent were disqualified. A further 3 percent were lost in the advanced rate training school. A total of 2,408 officers applied for training and of these 2,043 were graduated. It was found that Otis test scores obtained on enlisted men permitted a rough prediction of the general level of school performance, but gave only little more than chance prediction of rejections in training. Other tests are also discussed in the report. The officer qualification test was found to be a useful index for screening the officer candidates for submarine school.

In 1949 a study was reported by Cook and Wherry (*3455*) of the interrelationships of some 330 physiological and psychological measures obtained on a population of 120 submarine enlisted candidates. It was hoped by the authors that on the basis of this fundamental study it would be possible to establish a simple selection battery, consisting of the primary physiological and psychological factors which emerge significant. This could then be validated on a large, independent sample of applicants. In 1943 Graham, Riggs, Bartlett, Berry, Verplanck, Solomon, and Mueller (*3462*) reported a summary of research conducted at the U. S. Submarine Base, New London, Connecticut concerned with development of tests for identifying men who are unfit. Three criteria of unfitness were adopted: (1) psychiatric evaluation, (2) officers' judgment of men as operating crews of submarines, and (3) escape tank performance. The tests used were the NRC inventory, the New London-NDRC confidential questionnaire, the personal inventory, and a 2 hand coordination test. Data in the Otis intelligence test scores were also analyzed. The authors' report considered results obtained from 3 batteries, each made up of the 2 hand test and the Otis test in combination with one of the inventories. All of the individual tests related significantly to psychiatric criteria. The individual test combined with the New London and the personal inventory batteries, according to the procedure described, predicted the psychiatric dichotmy into good and bad in a highly significant degree and to an extent which improved considerably on results obtained by the intelligence test alone. A battery involving items of the New London inventory related significantly to officers' judgment of men from operating crews of submarines.

Graham, Mote, and Berry (*3461*) 1944 reported the relation of selection test scores to tank escape performance. In the course of escape training at the Submarine School, U. S. Submarine Base, New London, Conn. about 1½ percent of prospective submarine crew men were disqualified on the grounds of escape performance of an emotional type. A study of the relation of selection test scores to tank escape performance indicated that the test battery predicts tank failures to a degree considerably better than chance.

For reports describing and analyzing disqualification of enlisted applicants for submarine training, papers by Malinosky and Bartlett (*3469*) 1945, Bartlett (*3480*) 1946, and Shilling and Bartlett (*3481*) 1947 should be consulted.

Comparisons of various visual screening devices with standard medical procedures have been reported by the following: Farnsworth, Bartlett, and Kindred (*3459*) 1945; Farnsworth, Sperling, and Kimble (*3460*) 1949, and Sulzman, Farnsworth, Bartlett, and Kindred (*3484*) 1945. For an investigation of selection of candidates for enlisted submarine radar school a paper by Bartlett (*3448*) 1945 should be consulted.

For reports of studies on the development and validation of methods for the selection of sonar personnel, papers by Shilling (*3479*) 1942 and Harris (*3463*) 1946 should be consulted. The latter report gives a history of the submarine sonar selec-

tion program. For other reports the following references should be consulted: *3472, 3489,* and *3492.*

For a discussion of problems encountered in selection of submarine personnel in the French submarine service, a paper by Rosenstiel (*3477*) 1946 should be consulted. According to Curran and Critchley (*3458*) 1946 methods of selection for U-boat personnel in the German service were not essentially different from the undersea warfare services in other nations. The authors considered that morale in the German Navy generally appears to have been excellent and the incidence of breakdown low in comparison with other branches of the armed services in Germany. Deficiencies in neuropsychiatric practice were stated to be striking in the German Navy and the standard of available treatment low in comparison with that of other nations. For wartime selection standards for personnel in the Japanese submarine service, a report published by the U. S. Navy in 1945 (*3490*) may be consulted.

For reports on selection of Naval, Coast Guard, and Marine personnel, papers by the following may be consulted: Cornehlsen (*3456*) 1946; Leavitt and Adler (*3466*) 1946; McCain (*3467*) 1947–48; Newman, Bobbitt, and Cameron (*3473*) 1946; Rodger (*3475*) 1947; USNRC Committee on Dentistry (*3491*) 1949, and Williams, Leavitt and Blair (*3494*) 1946. For a few selected reports on selection and classification procedures in the U. S. Air Force papers by the following may be referred to: Buel and Melton (*3454*) 1943; McCollum (*3468*) 1951; Matthews (*3470*) 1943; Roff (*3476*) 1951. A number of reports on personnel selection, job assignment and personality tests have appeared and a few of these have been listed as follows: Alexander (*3444*) 1944; Bechtoldt (*3453*) 1951; Hunt and Stevenson (*3465*) 1946; Moore (*3471*) 1950; Richardson (*3474*) 1950; Rundquist (*3478*) and Shipley, Gray, and Newbert (*3483*) 1946.

For additional papers on selection, reports by the following may be referred to: Bartlett (*3446*) 1945, and Wiggin and Bartlett (*3493*) 1944.

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3450. Bartlett, N. R. Description of an abstract of the service record for analyses of examinations of experienced submarine personnel received for re-assignment. U. S. Navy. BuMed. *Project X–596* (*Sub. no. 128*), *Rept. no. 1,* 23 January 1946, 3 pp.

3451. Bartlett, N. R. Description of an abstract of the service record for analyses of examinations of experienced submarine personnel received for re-assignment. U. S. Navy. BuMed. *Project X–596* (*Sub. no. 128*) *Rept. no. 2,* 24 January 1946, 3 pp.

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3454. Buel, J. and A. W. Melton. The S. A. M. two-hand coordination test for the classification of aviation cadets: I. Apparatus and procedures. U. S. AAF. Randolph Field, Texas. School of aviation medicine. *Project 124, Rept. no. 1,* 11 March 1943, 10 pp. [P]

3455. Cook, E. B. and R. J. Wherry. A study of the interrelationships of psychological and physiological measures on submarine enlisted candidates: I. History, experimental design, and statistical treatment of data. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM–003–017, Rept. no. 1,* 9 March 1949, 45 pp.

3456. Cornehlsen, J. H., Jr. The selection and classification of naval officer personnel. *Amer. psychol.,* 1946, *1:* 349–352.

3457. Cronbach, L. J. Selection and training. pp. 491–513 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3458. Curran, D. and M. Critchley. German neuropsychiatry with special reference to the Kriegsmarine (and with a note on habitability of the Prinz Eugen). Gt. Brit. MRC–RNPRC, HS. *R. N. P. 46/320 H. S. 156,* August 1946, 37 pp.

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3485. U. S. Navy. BuNavPers. (A) Submarine personnel selection. pp. 135–142 in: *Submarine Medicine practice. NavPers 10838,* March 1949, 182 pp. [D]

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3487. U. S. Navy. Submarine base, New London, Conn. Medical research department. A comment on submarine personnel classification. *Project X–596 (Sub. no. 128) Rept. no. 3,* 28 January 1946, 5 pp.

3488. U. S. Navy. Submarine base, New London, Conn. Medical research department. Memorandum comparing the scores obtained by testing submarine school candidates with the Otis self-administering test of mental ability with the scores received on the general classification test, as recorded in the service records of these candidates. 28 December 1942, 10 pp.

3489. U. S. Navy. Submarine base, New London, Conn. Medical research department. Selection and training of sound listening personnel. 22 September 1942, 6 pp.

3490. U. S. Navy. Technical mission to Japan. Selection of personnel. pp. 39–40 in: *Aero, surface, and submarine medicine and research in the Japanese Navy. Fascile M–1, Target M–06,* 4 September 1945, 72 pp.

3491. U. S. NRC. Committee on dentistry. Minutes of the eighth meeting. 14 November 1949, 2 pp.

3492. Wever, E. G. and W. D. Neff. Classification of audigrams for use in the selection of sound operators. U. S. Navy. Submarine base, New London, Conn. Medical research department. 1 August 1942, 11 pp.

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3495. Willmon, T. L. Outline and discussion of methods for selection of submarine reserve personnel. U. S. Navy. Submarine base, New London, Conn. Medical research department. 16 February 1948, 16 pp. [R]

3496. Willmon, T. L. and N. R. Bartlett. Relationship of personnel selection devices to the behavior criteria of school performance and overall performance on a submarine patrol. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project X–243 (Sub. no. 47) Report no. 1,* 25 October 1944, 8 pp.

II. TRAINING

During World War II the training program operating within the submarine service reached an unbelievably high level of efficiency. Courses of instruction were developed, and techniques of training were perfected; new and improved equipment for training and indoctrination were instituted. The center of much of this training was at the Submarine School, U. S. Submarine Base, New London, Conn. However, training activity within the submarine force was located at almost every submarine base, notably Pearl Harbor.

That portion of the training program coming under the cognizance of the Medical Department is reviewed by Shilling and Kohl (*3502*) 1947. One of the most important training activities of submarine force candidates and personnel is the Escape Training Tank. Aside from the actual training value of the escape tank, an excellent means of selection is provided by this activity to eliminate those individuals not particularly suited for underwater activity. This particular aspect has been reviewed more completely in the foregoing section on selection (p. 299).

The submarine Escape Training Tank was designed to permit thorough training of all submarine personnel in the use of the "lung" or submarine escape appliance, under conditions which would simulate as closely as possible those prevailing during an actual escape from a disabled submarine. This 280,000-gallon tank contains a vertical column of water 100 feet high and 18 feet in diameter. Integrated with the tank are escape locks or compartments which duplicate those installed in submarines. These locks are located at depths from the top of the tank of 18 feet, 50 feet, and 100 feet, permitting escapes under conditions identical to those existing at similar depths at sea. All submarines are supplied with submarine escape apparatus and the crew must be properly trained in the use of the lung, either at the tank located at New London or at the one at Pearl Harbor. Active submarine personnel must requalify every year at either one of these tanks at the 12-foot and 30-foot stops.

To escape from a sunken submarine, it is necessary that the pressure within the compartment from which egress is to be made be equalized with the outside water pressure. To do this, the compartment is flooded by admitting water through various valves; as the water rises, it compresses the air in the upper part of the compartment. When the water rises to the top of the escape door or telescope trunk, it creates a pressure within the compartment equal to the sea pressure. At this stage it is possible for the hatch or door to be opened by hand. After the pressure is equalized, the hatch is opened and a buoy with an ascending line is released through the open hatch and escape is made to the surface with the use of the "lung."

Qualification at the tank consists of the following essentials: (1) a pressure test of 50 lbs. per sq. in. in the recompression chamber; (2) a lecture on construction, operation, safety features, and precautions in the use of the "lung"; (3) shallow water training for confidence in breathing under water; (4) 12-foot training to attain proper relaxation and confidence; (5) 18-foot and 50-foot escapes to train in the use of the "lung" so that should he be called upon to use this device under stress, he could most effectively use its life-saving qualities.

It is of particular interest that the sumarine service was the first in the U. S. Navy to inaugurate night lookout training and that this training was developed under auspices of the Medical Research Laboratory at the U. S. Submarine Base, New London, Conn. Also, the Medical Research Laboratory, through its advice, helped to modify the Navy's Recognition Program at Ohio State University so that night lookout training was combined with and added to all recognition training by the Navy.

Through this training a realistic horizon was provided upon which the trainee was required to sight and identify small ship models which were placed upon it. The apparatus provided also reproduction of distant gunfire, of moonlight, and of

recognition lights. Its advantages as a training device lay in its realism, and the interest which it aroused in the men. In operation, lookouts were posted in pairs and located and reported in proper phraseology the position and type of ships.

As a result of liaison work of the Applied Psychology Panel of the Office of Scientific Research and Development and the Medical Research Laboratory, U. S. Submarine Base, New London, Conn., the Telephone Talker School was officially established in July 1944. The name of this school was later changed to Interior Voice Communications School as it took over a broader field of instruction. One of the most important features of the training program was the teaching of the use of standard procedures, a type of practical drill which greatly facilitated instruction in voice communication procedures, phraseology, and terminology while simulating the actual operations. During the course the student participated in practical drills, torpedo approach, battle surface, and other standard patrol operations. An additional paper by Abrams, Miller, Mallory, Hibbitt, Temple, Neff, and Jenkins (*3497*) 1945 concerning submarine voice communication should be consulted.

For other general reports on training and the problems involved, the reader may consult articles by Bartlett (*3498*) 1946; Brown (*3499*) 1945; Molumphy (*3500*) 1949; Shilling and Kohl (*3501*) 1947; Verplanck (*3503* and *3504*) 1946; and Wolfle (*3505*) 1951.

3497. Abrams, M. H., J. Miller, L. A. Mallory, G. W. Hibbitt, W. J. Temple, W. D. Neff, and W. J. Jenkins. A project for standardizing submarine phraseology and developing a training program in submarine voice communications. Final report. U. S. OSRD–NDRC, *O. E. M. sr 658, 830, and 1128, Rept. no. 4795,* 28 February 1945, 31 pp.

3498. Bartlett, N. R. An evaluation of shipboard indoctrination of officer candidates for submarine training. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–531,* 5 February 1946, 11 pp. [R]

3499. Brown, W. B. The ship recognition trainer. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–271 (Av–159–c) First interval rept.,* 25 September 1945, 39 pp. [M]

3500. Molumphy, C. G. Report of diving training in U. S. S. *Chanticleer,* off Key West, during the period 19 October to 8 December 1948. U. S. Navy. Naval gun factory. EDU. *Project NS 186–042,* 1 July 1949.

3501. Shilling, C. W. and J. W. Kohl. Medical personnel. pp. 3–18 in: *History of submarine medicine in World War II.* U. S. Navy. Submarine base, New London, Conn. Medical research laboratory, 25 May 1947, 328 pp.

3502. Shilling, C. W. and J. W. Kohl. Training activities. pp. 32–62 in: *History of submarine medicine in World War II.* U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. 25 May 1947, 328 pp.

3503. Verplanck, W. S. Night lookout training stage. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–350 (Av–197–p) Final rept.* 1 March 1946, 14 pp.

3504. Verplanck, W. S. Experimental evaluation of the ship recognition trainer. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–271 (Av–159–c),* 14 March 1946, 10 pp.

3505. Wolfle, D. Training. pp. 1267–1286 in: *Handbook of experimental psychology.* Edited by S. S. Stevens. New York, John Wiley & Sons, Inc., 1951, 1362 pp. [M & R]

III. PERFORMANCE—SUBMARINE OPERATIONS

For a definitive report on United States submarine operations in World War II, reference should be made to the excellent and comprehensive volume by Roscoe (*3512*) published in 1949. In this exhaustive study of submarine operations many glimpses into human factors and their bearing on operational results are given. The author has presented numerous examples of performance of personnel under hazardous conditions and has discussed the almost mystical bond that welds submarine crewmen together. The relationships between skippers and their crews are illustrated by many stories. Closely related to morale are seen to be various psychological aspects of living aboard submarines. Most submariners find it more difficult to take severe depth charging when lying helplessly on the bottom than when maneuvering to evade. The command "battle surface" is sounded as a welcome break in the routine. The author stresses the psychological advantage of air-conditioning. Habitability of the submarine is discussed in many places in the volume and there is a consideration of the recouperation program during periods of leave. Weather conditions affected the men greatly and the worst conditions were said to be in the cold climate of the Aleutian Islands. The color of the interior of the submarine is considered to be of great importance. Submarine rescue work is referred to. The author states that 504 airmen were rescued by submarines during World War II. The work of hospital corpsmen attached to submarines is praised many times. Accounts of appendectomies performed by hospital corpsmen are given.

For a section on the history of the development of submarine warfare, reference should be made to Cope and Karig's volume (*3506*) published in 1951. In summing up battle operations the authors point out that odds were never better than even. That so many of our submarines survived scores of battles deeper into enemy territory than even aircraft could penetrate except during the last phases

of the war is testimony to the skill and resourcefulness of the young Americans who manned them from the bridge to the galleys. In a popular article Schwed and Wolters (*3513*) 1949 have pictured the U. S. S. Tusk inside and outside during a cruise. Life in a midget submarine in the British Navy has been described by Galway (*3509*) 1947. These midget submarines of the British Navy, spoken of as X-craft, spent many hours submerged reconnoitering off the Normandie beaches on D-day. Three British X-craft torpedoed the giant German battleship, Tirpitz in a Norwegian fjord. The author describes the effects of hypoxia and carbon dioxide in midget submarines. He points out that when surfaced after a 10-hour dive one usually got headaches. The rule while submerged was to avoid exertion and lead a languid existence. Food was cooked in an electric pot and electric kettle. Most of the meals consisted of sandwiches washed down with orange juice or condensed milk. The toilet was situated in the escape chamber and known as "wet and dry" because it could be flooded and pumped dry at will. It was hardly ever dry. It was described as an unsalubrious spot in which there was little temptation to dally and only just room to move. The tank was pumped out only at night. Washing was limited to shaving and brushing the teeth. Many men took a swim at night to get clean. The first lieutenant of one of the boats indulged in a swim overside during the Tirpitz adventure. Members of the crew became accustomed to each other's odor and tended to be avoided by submarine tender crews until they had taken a bath. The inside of the boats was wet with condensation from hot drinks and water brought by men from the watch into the interior. There were meager bunking facilities in the battery room and the engine room. The bunk in the control room was usually filled with food supplies.

The Germans made use of three different types of midget submarines (*3514*). These were the "Biber," the "Molch," and the "Seehund." The "Seehund" was the largest of the midget submarines and was prefabricated with an overall length of 39 feet, a depth of 6 feet, and a displacement of about 16 tons. This craft had a surface speed of 8 knots and a submerged speed of 3 or 4 knots. Propulsion was by diesel engine and electric motors. The "Seehund" carried two 21-inch modified electric torpedoes. The range of the submarine at 8 knots was 275 miles plus 50 miles at 3 knots submerged. The "Biber" was the smallest of these submarines and was a one-man boat. Its overall length was 29½ feet with a beam of 4 feet 9 inches. It was equipped with 2 outboard torpedos. In this submarine the pilot conned through 6 rectangular armoured glass scuttles. The hatch was also fitted with a glass scuttle for upward observation. At normal trim the conning tower rose about 2 feet above the water and was fitted with a projector compass about 18 inches in height, a periscope 4 feet 6 inches in height and an air intake. The boat was propelled by a gasoline engine and an electric motor and the air intake was designed so that the submarine could proceed on her engines with the hatch closed. The maximum speed was 6½ knots, the submerged speed being 6 knots. The maximum endurance was 48 hours or 100 miles. The submarine operated to a depth of 60 feet. The "Molch" was a one-man submarine 46 feet long and 7½ feet deep. Its armourment was similar to that of the "Biber."

For other reports on performance, the reader may consult the section on general studies of submarine medical problems (p. 1) and the section on diseases and accidents in naval personnel, morbidity (p. 149). For reference to manuals and textbooks issued to pharmacist's mates on submarines, the following items in the bibliography are given: *3508, 3510,* and *3511.*

For an excellent and graphic study of the job carried out by tunnel diggers, a paper by Corcoran and Wolters (*3507*) 1947 should be read.

3506. Cope, Harley, and Walter Karig. The submarine. pp. 3–16 in: *Battle submerged. Submarine fighters of World War II.* First edition. New York, W. W. Norton & Company, 1951, 244 pp.

3507. Corcoran, J. and D. Wolters. The tunnel diggers. *Sci. Ill.,* 1947, *2:* 50–59.

3508. Cullen, Stuart C. and E. G. Gross. *Manual of medical emergencies.* Chicago, The Year Book Publishers, Inc., 1949, 267 pp.

3509. Galwey, G. V. Life in a midget submarine. *Proc. U. S. nav. Inst.,* 1947, *73:* 421–425.

3510. Jensen, Julius and Deborah MacLurg Jensen. *Nursing in clinical medicine.* Third edition. New York, The Macmillan Company, 1949, 791 pp.

3511. Rehfuss, Martin Emil and Alison Howe Price. *A course in practical therapeutics.* Second edition. Baltimore, The Williams & Wilkins Company, 1951, 938 pp.

3512. Roscoe, Theodore. *United States submarine operations in World War II.* U. S. Naval Institute, Annapolis, Maryland, 1949, 577 pp.

3513. Schwed, W. W. and D. Wolters. Snorkel, submarine that breathes. *Sci. Ill.,* 1949, *4:* 34–41, 86.

3514. Anon. German midget submarines. *Engineer, Lond.,* 1945, *179:* 428–429.

IV. SPECIAL SONAR PROBLEMS

The submarine acquires information about its environment by various methods: visual contact, radar, radio, and sonar. Sonar utilizes sound waves which are transmitted through water, the sound

signals being picked up from the water, amplified, and finally analyzed in various ways. These are presented to the operator as useful items of information about objects and their movements in the water around them. The submarine is made aware of the position of floating mines and the position, type, speed, and course of a surface vessel or another submarine.

The sound man using sonar apparatus must detect a sound signal presented to him in a background of noise. The signal will differ from the background in one or more of the following characteristics: rhythm, loudness, and quality. Capacity for rapid and successful differentiation of changes in these characteristics of auditory signals determines to a great extent the success of the sound man and the life of the submarine. Therefore, improvement of selection procedures will depend immediately upon answers to auditory problems arrived at through psycho-physical studies. Solutions to the more far-reaching problems will depend on physiological information.

For an excellent description of auditory problems arising out of sonar operation, a chapter by Neff and Thurlow in the monograph, *Human factors in undersea warfare,* National Research Council, Washington, D. C., 1948, should be consulted. Other chapters in this monograph are referred to elsewhere (1726 and 1737). Auditory tasks of the sonar operator, methods of investigation, and results of relevant research and suggestions for future research are discussed. Experimental evidence provided in a paper by Harris (*3517*) 1945 has shown that 0.27 decibels is the negative time-error for an average group of subjects. For poor subjects the magnitude of the negative time-error was 0.6 decibel. No sound change was reported from subjects presented a standard sound stimulus, the signal then being increased or decreased 0.28 decibel in intensity. No correlation was found to exist between the test and final sound school grades but when correlated against specific auditor sonar performance to which loudness discrimination may reasonably be presumed contribute, correlations of the order of 0.21 to 0.51 were obtained. Significant differences in performance were found between those who do poorly and those who do average or better on the test.

Additional data obtained by Myers and Harris (*3520* and *3521*) 1948 indicates that a zone of detectability of the order of two to three decibels exists between the intensity at which a tone is just detected 50 percent of the time and the intensity at which it may be assigned a pitch quality 50 percent of the time. This zone where some unidentified sound can be heard is somewhat less for the medium tones. The zone of detectability of the frequencies 500, 1,000, 2,000, 4,000, 8,000, and 14,000 cycles per second varied at random from 2 to 4 decibels, independently of frequency. For the higher frequencies, an experienced subject can select a certain criterion of tonality and maintain it with considerable precision. The matching of variable frequencies of low sensation levels to a standard frequency of 10 decibels showed improvement in matching as the intensity increased from 0 to 10 decibels. It was reasoned that the subjective criterion of tonality which a subject can select and maintain is one of pitch rather than of loudness. The authors concluded that the phenomenon depends upon the intensity of the stimulus rather than upon a change in its frequency composition.

Group audiometry, as contrasted to individual auditory testing, was tried and evaluated by Myers, Harris, and Fowler (*3522*) in 1948. Complete audiometric examinations were given to 1448 men in seven days. It was found that with a college population, the group technique is effective within a two percent error. Effectiveness of this examination procedure requires a psychological impetus which will force the subject to use his last 10 decibels of hearing ability. A history of childhood disease was found to be slightly related to high-tone deafness and of the 94 men who had had aerotitis media, 5.3 percent had a low-tone average loss of 25 decibels. Aerotitis media contributes slightly to high tone loss.

For further reports on special sonar problems, papers by the following may be consulted: Harris (*3515*) 1944; (*3516* and *3518*) 1945; and (*3519*) 1946; Neff (*3523, 3524,* and *3525*) 1942; Schafer (*3526*) 1949; U. S. Navy (*3527*) 1942 and (*3528*) 1946; and U. S. National Research Council (*3529*) 1950.

3515. Harris, J. D. Propeller noise discrimination. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Preliminary report, Project X–53,* 26 December 1944, 14 pp.

3516. Harris, J. D. Functions of pitch in submarine sonar operation. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project X–330 (Sub. no. 59)*, 30 January 1945, 15 pp.

3517. Harris, J. D. Functions of loudness discrimination in submarine sonar operation. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Interval report, Project X–53,* 5 April 1945, 19 pp.

3518. Harris, J. D. The relation between the audiogram at high frequencies and proficiency in sonar performance. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Interim report no. 1, Project X–329 (Sub. no. 58)*, 4 June 1945, 9 pp.

3519. Harris, J. D. Comprehensive validation of submarine sonar selection tests. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Final*

report on Projects X–327 (*Sub. no. 56*), *X–330* (*Sub. no. 59*), *X–331* (*Sub. no. 60*), *X–632* (*Sub. no. 137*), 30 September 1946, 32 pp.

3520. Myers, C. K. and J. D. Harris. Detection thresholds and pure tone thresholds in auditory acuity. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM–003–022* (*X–747* (*Sub. no. 154*)) *Rept. no. 2,* 22 January 1948, 7 pp.

3521. Myers, C. K. and J. D. Harris. The emergence of a tonal sensation. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory. *Project NM–003–022, Rept. no. 4,* 31 March 1948, 14 pp.

3522. Myers, C. K., J. D. Harris, and E. P. Fowler, Jr. The feasibility of group audiometry. U. S. Navy. Submarine base, New London, Conn. Medical research department. *Project NM 006 007* (*X–761* (*Sub. no. 163*)) *Terminal report,* 12 February 1948, 54 pp.

3523. Neff, W. D. Memorandum on the selection and training of sound operators. U. S. Navy. Submarine base, New London, Conn. Medical research department. 7 July 1942, 43 pp.

3524. Neff, W. D. Memorandum on test-retest reliability of pitch discrimination tests. U. S. Navy. Submarine base, New London, Conn. Medical research department, 14 December 1942, 2 pp.

3525. Neff, W. D. Memorandum on inventory of musical background, Form B. U. S. Navy, Submarine base, New London, Conn. Medical research department. 15 December 1942, 4 pp.

3526. Schafer, T. H. Detection of a signal by several observers. U. S. Navy, NEL, San Diego, Calif. *U. S. N. E. L. Rept. no. 101,* 26 January 1949, 9 pp.

3527. U. S. Navy. Submarine base, New London, Conn. Medical research department. Memorandum on an abbreviated procedure for the determination of audiograms in the selection of sound operators. 1 August 1942, 3 pp.

3528. U. S. Navy. NEL, San Diego, Calif. Studies of the recognition of submarine echoes. *Contract NObs–2074, File no. 01–41,* 30 September 1946, 108 pp. [R] [P]

3529. U. S. NRC–CUW. Panel on underwater acoustics. A survey report on basic problems of underwater acoustics research. 1950, 137 pp.

Special Psychological and Psychiatric Problems

I. GENERAL STUDIES

Two items are listed as general source material on military psychological problems. The first is a monograph published by Bray (*3530*) in 1948. This work constitutes a history of the applied psychology panel of the National Defense Research Committee. The second item is a survey report on human factors in undersea warfare published by the National Research Council in 1949. In addition, Kennedy's chapter (*3531*) on personnel resources for research in *Applied Experimental Psychology* may also be consulted.

It has become increasingly apparent in modern times that the peculiar complexity of military operations in general and submarine warfare in particular creates psychological problems which can no longer be successfully handled haphazardly or without recourse to special skills available to the discipline of psychology. Some of the special problems include those arising in selection and classification of personnel, training, performance, and the design of controls, displays, and work spaces to conform to human capacities and limitations. Present and projected submarine operations impose excessive stress on personnel under certain conditions and problems of fatigue and morale take on new significance. Questions of sleep-wakefulness cycles and duty and rest periods can no longer be left unanswered or handled by chance alone. There seems little doubt but that if adequate attention is given to human factors in submarine operations with proper consideration for habitability and good morale, the incidence of psychiatric breakdown may be kept at a minimum.

3530. Bray, C. W. *Psychology and military proficiency. A history of the applied psychology panel of the national defense research committee.* Princeton, Princeton University Press, 1948, 235 pp.

3531. Kennedy, J. L. Personnel resources for research in applied experimental psychology. pp. 517–518 in: *A survey report on human factors in undersea warfare.* Washington, D. C. National Research Council, 1949, 541 pp.

II. HUMAN FACTORS IN ENGINEERING DESIGN

This section, although focused on the submarine, covers material not limited to this branch of the service, either for experimental data or applications. Industry and the allied military services have contributed much information relative to the problem of instrument, control, and panel design as they apply to the human operator. For example, research on cockpit design for aircraft has a relation to the design of submarine control rooms and systems research on the CIC for surface ships applies also to submarines.

In a control system, man has been regarded as a chain consisting of sensory devices, a computing system to reduce misalignments on the basis of previous experience, an amplifying system rendering small afferent nerve activity effective to initiate muscle action, and finally a mechanical linkage system. Craik (*3546*) 1948 also states that the primary problem of human engineering consists in discovering in detail the characteristics of this human chain as it compares to an automatic system. Although satisfactory data on many human engineering design problems have been gathered, Stellar (*3581*) states that many of the gaps have been filled in rather liberally with opinions and hypotheses. There has been a tendency of the literature in this area to formulate general principles of panel design prematurely and to offer them as recommendations to the design engineer. Actually it has turned out that many of these principles are little more than the common sense opinions of experienced engineers and psychologists. Keeping in mind the need for separation of fact from opinion, the author lists 6 general principles which one should try to adhere to in planning panel layouts: (1) All controls and displays should be located within a practical working distance from the operator.

(2) Within the working area, each control and display should be situated in a position where it may be most efficiently used. (3) Where two or more controls or displays on a panel have the same optimal position, the more important and more frequently used items should be given the preferred positions. (4) Controls and displays should be grouped in patterns that make for the easiest operation and observation from the point of view of the operator. (5) No one part of the body should be overloaded with work that could be assigned to other body parts. (6) Any possible confusion of controls or of displays by the operator should be avoided by proper design or placement.

For additional general studies of human engineering design, papers by the following should be consulted: Bartley and Chute (*3533*) 1947; Channell and Tolcott (*3536*) 1948; Chapanis (*3537*) 1951; Fitts (*3553*) 1949; Lawrence (*3564*) 1946; Mackworth (*3569*) 1949; and Tufts College (*3582*) 1949.

The sensory signal is presented to the operator by instrument dials or gages. The problem of design for each type of instrument is somewhat special, in terms of the way in which the information is presented or the varied conditions under which it will be used. According to Kappauf (*3561*) 1949, there are in general, two kinds of instruments: one which proposes to be accurate and quantitative, the other, a monitoring or checking type of instrument. Readings from either type of instrument should conform with stated tolerances or operating requirements. How well these tolerances are met depends upon the restrictive nature of the conditions of instrument use and on the adequacy with which display design variables have been manipulated to take particular account of the operator's characteristics. Two different types of instrument reading conditions are recognized in submarine service: (1) Some instruments must be illuminated in such a way that the operator and his neighbors will remain as well dark-adapted as possible for night observation. (2) Other instruments are used at stations where operator dark-adaptation is not a consideration and so these indicators and devices may be well illuminated. The author discusses problems of instrument marking, instrument illumination, instruments for presenting quantitative data, check reading instruments, and design of specific instruments.

Experimental observations by Kappauf (*3562*) 1951 indicated that the best design for a simple dial numbered every 10 units and quantitatively at any and all scale values, is one which has a scale break at zero, locates the zero near the bottom of the dial, and locates the numbers outside the scale. Additional data by Kappauf (*3563*) 1951, obtained on 20 subjects reading a series of simply designed, straight scales, graduated every unit and numbered every 10 units, demonstrated that reading to the nearest unit as compared to reading to the nearest 10 unit required about 1½ seconds additional reading time. In addition to this there were about 50 percent more reading errors.

For a complete discussion of visual displays, the reader should consult the lengthy monograph by Chapanis, Garner, and Morgan (*3538* and *3539*) 1949. It is stated that a direct-reading counter is better than a circular scale. Markers that change in value from one part of the scale to another or from one dial to another have been found to be very confusing. To increase accuracy and decrease the number of errors, a scale should increase from zero in a clockwise direction.

Poulton (*3578*) 1950 investigated the effect of practice on the accuracy of tracking with a two-pointer display as compared with a one pointer display. Results of the investigation provided confirmation of the prediction that performance with a one pointer display could be improved by presenting the subject with additional information. It was found that practice resulted in a relative improvement in tracking with a one pointer display, principally because the subject showed so little anticipation initially with the one pointer. Learning with one pointer displays could be accelerated by presenting the subject from time to time with an additional pointer showing the "stimulus" movement. For further studies on instrument design and dial legibility, reference may be made to papers by Barber and Garner (*3532*) 1951; Chapanis and Leyzorek (*3541*) 1950; Crook, Harker, Hoffman, and Kennedy (*3549*) 1948; Fitts (*3554*) 1951; Loucks (*3566, 3567,* and *3568*) 1944; Saltzman (*3579*) 1950; and White (*3590*) 1951.

As has been stated, two different lighting situations exist in the submarine. The conditions under which low levels of illumination are needed to preserve night vision in the submarine were investigated by Lee and Finch (*3565*) 1945 at the Naval Medical Research Institute at Bethesda. It was decided that red light of wave lengths longer than 590 units should be used in submarine conning towers during night operations. Patches of red light may be used to locate instruments and hatches if the intensity is kept below 0.003 millilamberts. Instrument markings should be red on a black dial and the intensity of numbers which subtend 18 minutes of arc by 14 minutes of arc at the observer's eye may be set as high as 0.003 millilamberts without disturbing night vision, provided the ratio of

luminous to total dial area is less than one-tenth. At this intensity the dial numbers will be clearly visible to a light adapted observer as well as to a dark adapted person.

The experimental results obtained by Chalmers, Goldstein, and Kappauf (*3535*) 1950 from 8 subjects reading 12 different types of dials at various levels of illumination indicated a progressive increase in the number of errors as illumination decreased. Gross errors and reading times changed very little with decreasing brightness until a critical level was reached. This level was found to be equivalent for all dials with a given size of lettering. Additional data on the effect of illumination on dial legibility can be obtained from papers by Crook and Baxter (*3548*) 1951; Gleason (*3558*) 1947; Partridge and Solandt (*3575*) 1943; Spragg (*3580*) 1948; and Wise (*3591*) 1948.

Reacting to adequate auditory or visual stimuli, the operator may have to make adjustments with hand or foot controls. Although the control system in some instances may consist of only one single element, more often it consists of a number of elements linked together. The designer's choice therefore depends to a great extent on the nature of the task which the system must perform. A complete discussion of the factors relating to control design is provided in a paper by Craig and Ellson (*3544*) 1949. Traditional attempts to link a better man to the machine and, through changes in existing equipment, to provide a better link between man and machine, have masked the fact that the operator and his controls are transmission elements in the control system and that the control task is performed by the control system as a whole. The designer of control systems needs to know the transmission characteristics of the operator, his operating ranges, and his susceptibility to expected operating conditions. The designer must constantly be reminded of the fact that "the operator" as an element in the design of the system is an abstraction from the operator who, as an individual, is the embodiment of a multiplicity of transmission systems.

Chapanis, Garner, and Morgan (*3540*) 1949 emphasize the importance of selecting appropriate controls for the task and the use of controls which are psychologically realistic. Controls should be adjusted not only to the force which operators are able to exert but also for values at which changes can be discriminated. Remarkable increases in efficiency can result from adjusting the ratio between control movement and indicator movement.

A study of positioning reactions involving movements from a point of rest to a terminal position at varying distances was carried out by Brown, Knauft, and Rosenbaum (*3534*) 1948. The reactions were made in total darkness after a 2.5 second visual presentation at one of the following positions: 0.6, 2.5, 10, or 40 cm. distant. Various planes of movement were studied. It was found that a greater variability occurred in positioning movements directed away from the body when compared to those movements directed toward the body at distances of 10 and 40 cm. The relationship was reversed for distances of 0.6 and 2.5 cm. This effect is attributed to the position of the terminal points with respect to the body, since the larger variabilities were associated with the more remotely located points.

Studies by Weitz (*3587* and *3588*) 1944 and (*3589*) 1945 indicated that changing the position of controls and shape of handlers in transfer tasks had the greatest detrimental effect on speed and accuracy of performance. Changing position alone produced some loss in performance whereas keeping the position of the controls constant but varying the shape of the handles showed practically no loss in performance. Following learning of control positions, changing of these positions was found to have detrimental effects on speed and accuracy of performance. This effect is minimized to a degree when the control handles are coded with respect to color and shape. For additional papers on design of controls, reports by the following may be referred to: Clutton-Baker (*3542*) 1951; Helson (*3559*) 1949; Jenkins (*3560*) 1947; and Mitchell and Vince (*3570* and *3571*) 1951.

The human operator is usually included as a matter of necessity rather than choice. If the designer is to include the operator in the design, he will require the same sort of information about the operator as he does about the other elements. He will need to know his operating characteristics and limits and his susceptibility to task conditions. Craik (*3545*) 1947 describes the place of the operator in control systems. The human operator behaves basically as an intermittent correction servo. This is evidenced by the periodic or "wavy" nature of a time record of tracking errors showing a spectrum with a predominant frequency of about 0.5 seconds and a smaller cluster of frequencies from 0.25 to 1.0 second.

Reference may also be made to a report from Tufts College (*3584*) 1949 on motor responses involved in control systems. The stimulus which evokes motor responses usually involves some type of sensory discrimination and this can be either visual, auditory, tactual, kinesthetic or combinations of any of these. The basic factors involved in motor responses are reaction time, speed, force, and precision.

A review article by Conrad (*3543*) 1951 discusses the principles involved in skilled behavior. It is believed that varying the nature of one motion element of a cycle alters the time taken for the remaining element. The visual requirements of a task are the predominant factors determining optimum conditions. These visual requirements can be slightly modified after the task has been become a habit because the eyes leave the scene of action before the action is completed.

A number of reports may be consulted on the general aspects of the physical and physiological characteristics of the human operator acting as a transmission unit in the control system. Items by the following authors have been selected because of their special bearing on this subject: Darcus and Maynard (*3550*) 1951; Elbel (*3551*) 1945; Fisher and Birren (*3552*) 1945; Gagne and Foster (*3555* and *3556*) 1948; Gibbs (*3557*) 1951; Newman and White (*3572*) 1951; Norris and Spragg (*3573* and *3574*) 1950; Paulsen (*3576* and *3577*) 1935; Tufts College (*3583* and *3585*) 1949; and Weddell and Darcus (*3586*) 1947.

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3538. Chapanis, A., W. R. Garner, and C. T. Morgan. Instrument dials and legibility. pp. 118–156 in: *Applied experimental psychology,* New York, John Wiley & Sons, Inc., 1949, 421 pp.

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3543. Conrad, R. Study of skill by motion and time study and by psychological experiment. *Research,* 1951, *4:* 353–358.

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3546. Craik, K. J. W. Theory of the human operator in control systems. II. Man as an element in a control system. *Brit. J. Psychol.,* 1948, *38:* 142–148.

3547, Crook, M. N. Printed materials, maps, and charts. pp. 61–76 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3548. Crook, M. N. and F. S. Baxter. Recognition time for dial-type numerals as a function of size and brightness. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. no. 6465,* March 1951, 26 pp. [P]

3549. Crook, M. N., G. S. Harker, A. C. Hoffman, and J. L. Kennedy. Studies of the effect of typographical spacing on the legibility of numerals under vibration. USAF. Wright-Patterson air force base, Dayton, Ohio. Aero medical laboratory. *Technical rept. no. MCREXD–694–10,* 23 September 1948, 18 pp. [P]

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3583. Tufts College. Anthropometrics. 8 pp. in: *Handbook of human engineering data for design engineers.* Tufts College. Institute for applied experimental psychology. *SDC Human Engineering Project 20–G–1, Project Designation NR–783–001, Technical Report 199–1–1,* 1 December 1949, 410 pp.

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III. PSYCHOMOTOR RESPONSES

Of the extensive literature on psychomotor reactions only a small number of papers have been selected. Lewis' report (*3595*) on the double-disk pursuit apparatus for studying interference in psychomotor performance may be consulted. Reference may also be made to a report by Poulton (*3596*) 1950 on anticipation in sensorimotor skills. By anticipating thc time of occurrence of a signal the subject can make the appropriate response synchronously with the signal. A classification of sensorimotor skills into open and closed types is suggested by the author, the position of any particular skill on this continuum depending upon the degree of predictability of the environmental signals. One advantage of closed skills is the reduced attention which environmental signals require. A second advantage, shared by open skills allowing receptor anticipation, is that voluntary compensation is seldom required. In a report on speed and load stress in a sensorimotor skill, Conrad (*3593*) 1951 found with all loads an increase in speed of signals gives a statistically significant increase not only in the absolute number of errors but also in the proportion of presented signals which are missed. Increasing the speed 3 times increased the errors at least 30 times with the 4 dial displays used in the apparatus with which these studies were carried out. Without altering the number of signals per minute, doubling the load much more than doubled the number of errors of omission. Therefore, the author concluded that load alone is an important factor in skilled deterioration. Of the responses made, the size of errors of timing is not affectcd by the speed of the task. Doubling the load approximately doubles the timing error. The subjects were never asked to deal with more than two series of events although there is no obvious theoretical justification for this limit. The author states that little is known of psychological functions that underlie the ability to perceive selectively, to ignore some signals, to store others, to combine yet others, and to withhold responses until the critical moment. Not much is known about the factors that disturb the operation of thcse functions.

That operation of a pursuit meter represents a stressful situation reflectcd in the lymphocyte response and the output of 17-ketosteroids is indicated by Hoagland, Elmadjian, and Pincus (*3594*) 1946. In these studies, three normal men, three normal women, two cooperative, schizophrenic patients and one cooperative psychopathic patient operated the Hoagland-Werthessen pursuit meter breathing a 12 percent oxygen mixture with the carbon dioxide absorbed. It was found in the normal subjects that the lymphocyte count fell with the stress of the experiments, whereas in the case of the patients it generally rose with the stress. In the normal group, the stress was shown to increase the output of 17-ketosteroids as it lowered the lymphocyte count. The patients revealed anomolous changes in 17-ketosteroid output.

In 1944, Brown (*3592*) discussed the use of psychomotor tests in the selection of radar operators. He pointed out that the principal psychomotor aspect of radar operators' tasks appears to be the ability to memorize and perform several complex series of rather precise manual actions. Although few of the individual actions are inherently difficult, the psychomotor complexity arises from the necessity for performing them in the correct order with speed and precision. In certain instances the actions involvc coordinated preceptual judgments and clear conceptual standards of what constitutes accurate judgment.

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3595. Lewis, D. Devices for studying interference in psychomotor performance: III. The double-disk pursuit apparatus. State University of Iowa. *SDC Human Engineering Project 20–M–1, Project NR–783–002, Rept. no. 57–2–13,* undated, 18 pp.

3596. Poulton, E. C. Anticipation in open and closed sensorimotor skills. Gt. Brit. MRC. The psychological laboratory, Cambridge. Applied psychology research unit. *A. P. U. 138/50,* September 1950, 18 pp.

IV. PSYCHOLOGICAL FACTORS IN PERFORMANCE

It has frequently been observed that under certain emergency circumstances combat personnel rise above various adverse environmental conditions and perform at an unusually high level of competence, at least for a limited period of time. The exact nature of the psychological factors in such performance is not known. Mackworth (*3599*) 1947 has approached the problem by investigating the question as to whether high incentive will enable men to surmount difficulties of working in hot and humid atmospheres and satisfactorily complete a series of tasks. In laboratory experiments he chose the task of lifting and lowering a 15 lb. weight by bending and straightening the arm in time to a metronome. The subject was to continue this task until completely exhausted. High incentive was provided by letting him have the results as he worked and giving a running commentary of encouragement. Powerful incentive failed to delay deterioration in physical output when the men were working to complete exhaustion in high atmospheric temperatures. High incentives failed to alter the critical level on the room temperature scale above which performance began to deteriorate. However, the incentive used did greatly raise the total output of work. Extra incentives were particularly effective with the better subjects. The performance increase was found to be larger when the atmospheric temperature was normal than when unusually high.

For other reports on psychological factors in performance, papers by the following may be consulted: Cane and Horn (*3597*) 1951; Gibbs (*3598*) 1951; Seashore (*3600*) 1951; and Vince (*3601*) 1948.

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3598. Gibbs, C. B. Transfer of training and skill assumptions in tracking tasks. *Quart. J. exp. Psychol.*, 1951, *3:* 99–110.

3599. Mackworth, N. H. High incentives versus hot and humid atmospheres in a physical effort task. *Brit. J. Psychol.*, 1947, *38:* 90–102. [P]

3600. Seashore, R. H. Work and motor performance. pp. 1341–1362 in: *Handbook of experimental psychology.* Edited by S. S. Stevens. New York, John Wiley & Sons, Inc., 1951, 1362 pp. [M] [R]

3601. Vince, M. A. The intermittency of control movements and the psychological refractory period. *Brit. J. Psychol.*, 1948, *38:* 149–157. [P]

V. STRESS

For a detailed report of the effects of combat stress, the important monograph of Grinker and Spiegel (*3606*) 1945 should be considered. These authors have differentiated two groups of psychological casualties. In the first, minimal stress has produced severe symptoms due to previous emotional disorders which lessen psychological preparedness. In the second group, severe stress has produced symptoms only after long exposure in men who are psychologically stable. The authors give histories of cases where previous disorders have rendered men incapable of withstanding combat stress. The authors define operational fatigue as "a reactive state in which the ego loses power to control intense anxieties and hostilities and to maintain functional efficiency". The symptoms of combat fatigue are varied and are classified as free anxiety states, phobic states, conversion states, psychosomatic reactions, and depressions. Treatment of combat reactions in the theaters of operations fell into two phases: first, the prevention and early treatment at the level of the combat group and, second, removal of the individual from the combat organization for definitive psychiatric care. In the Army Air Force the flight surgeon was accorded responsibility for the first phase while psychiatric consultants took responsibility for the second. The flight surgeon, like the family doctor, bears a heavy responsibility for the general welfare of the men. He is an important contribution to the success of the mission and he must have a thorough understanding of himself and a familiarity with the problems facing his men. Early handling of psychiatric casualties involves an attempt to increase insight, to neutralize ineffective or crippling methods of dealing with anxiety, to permit abreaction of anxiety and hostility, to modify the superego, to support dependent needs, and to estimate the limits of tolerance for anxiety. When these attempts fail prompt removal of the individual from the combat group becomes necessary. The problem facing the psychiatrist is a difficult one. He must decide whether the patient is able to tolerate further combat stress and whether with further psychotherapy he can be returned to combat in a short time. If this is not possible, it must be decided whether he can carry out a new assignment in flying or on the ground. A decision may also have to be made whether the patient should be returned to the zone of interior for prolonged treatment. While the authors have discussed these problems from the point of view of combat flying, their experience and conclusions bear significantly on submarine warfare as well.

Haggard (*3607*) 1949 has analyzed those factors which determine the effects of stress on the individual, particularly in submarine operations. The author stresses the importance of the childhood de-

velopment of the individual, his reactions to his parents, siblings and others. A necessary aspect of military life in general and of submarine operations in particular is the relationship between the officers and the enlisted men. The officers give commands, exert dominance, and look out for the men, who in turn take orders and are dependent on the officers. Both must be able to assume their proper roles. As a rule the greater the emotional stress experienced by all members of the submarine group, the more they become fused together into a group and the more the welfare of the group supersedes that of any one individual. Often men who had traumatic childhood experiences or histories of neurotic difficulties did not break down under the stress of battle.

Haggard stresses that in an emergency where an individual's welfare, safety, and integrative capacities are threatened, he mobilizes energy to cope with the threat whereby he may escape or, if properly directed, will fight effectively. If aggressive impulses do not find adequate outlet they express themselves in chronic anxiety, fatigue, accident proneness, or physical illness. It is difficult and enervating to do nothing when one is stimulated to activity, as being compelled to submit to depth charging without being able to do anything about it. As a person becomes progressively adapted to a stress situation, he learns that by keeping his head he will subject himself to minimal danger and will be able to react more effectively than otherwise. Realistic training under realistic conditions is a necessary procedure in the prevention of psychiatric casualties in combat. Breakdown may occur after the stress situation is over and may be due to relaxation of the person's defense against aggressive impulses and a return, in overwhelming intensity, of anxiety previously held in check. Emotional stress is intensified where cognitive structure is lacking. To have been through an experience and to have executed duties successfully usually imparts self-confidence and enhanced efficiency to a man. Motivation is also brought out as a critical factor in the individual's adjustment to emotional stress. Undesirable motivations found in unstable, highly egocentric individuals stem from the desire to escape from something distasteful or to gain status and self-respect through short cuts. Emotional strain may also result from a conflict of motives. Situational conditions may also precipitate collapse of the individual's adjustive mechanisms. For instance, he may be caught off guard after a series of moderate stimuli or by the presentation of stimuli which recurred too frequently or for too long to permit adequate rest. Strict adherence to a highly rigid time schedule or forced delay of a response after the signal to act is given or being forced to alternate between action and restraint may all be factors in breakdown.

Darrow and Henry (*3604*) 1949 have given a report on the psycho-physiology of stress in submarine activities. They describe severe physiological responses to environmental conditions such as oxygen deficiency, carbon dioxide excess, high temperature, odors, etc. They also call attention to stresses imposed in the performance of duty involving fatigue, loss of sleep, and hunger. Emotion under stress, as in depth bomb attacks, may result in combat fatigue. Finally, factors such as boredom, poor morale and so forth may aggravate the other effects of stress. The authors describe several means of recording and evaluating emotionally-induced organic changes which may be symptomatic of effects within the central nervous system. These include studies of the electromyogram, the galvanic skin reaction, blood pressure, heart action, respiration, blood oxygenation, vasomotor changes in the extremities, blood sugar, metabolic activity, endocrine function, electroencephalographic action, etc.

Performance of psychomotor and other psychological tests may be significantly altered under conditions of stress and experimental studies of such alterations have been carried out. An example of such studies is that by Vince (*3615*) 1950 on learning and retention of an unexpected control-display relationship under stressful conditions.

A familiarity with the work of Selye is essential for an intelligent examination of the responses to stress. The following references to Selye's work are given: (*3610*) 1946, (*3611*) 1950, and (*3612*) 1951. Apart from many specific defense reactions to stress there is an integrated syndrome of closely interrelated adaptive reactions to nonspecific stress itself. This has been termed by Selye the "general adaptation syndrome". This syndrome may be defined as the sum of all nonspecific systemic reactions of the body which ensue upon long-continued exposure to stress. It evolves in three distinct stages: (1) the stage of alarm reaction; (2) the stage of resistance; and (3) the stage of exhaustion. The alarm reaction is the sum of all known specific systemic phenomena elicited by sudden exposure to stimuli to which the organism is quantitatively or qualitatively not adapted. Sometimes two phases of the alarm reaction appear: (a) shock and (b) counter-shock. Most of the characteristic manifestations of the alarm reaction disappear or are actually reversed during the second stage—that of resistance. However, even a highly adapted organism cannot indefinitely maintain itself at the stage of resistance. If exposure to abnormal conditions continues the

adaptation fails and manifestations characteristic of the alarm reaction reappear and the stage of exhaustion develops. The references cited contain discussions of the various theories which have been advanced to explain the various stages of the general adaptation syndrome. The general adaptation syndrome never occurs in its pure form but is always complicated and modified by superimposed specific actions of eliciting stressors.

There is a considerable volume of literature on the effects of stress and emotional reactions upon heart rate, breathing, and arterial blood pressure. It appears that the cardiovascular responses in question vary in character, intensity, and duration according to the characteristics of the stressing situation and the personality structure of the individual. Two earlier papers on this subject are those of Landis and Gulette (*3608*) 1925 and Skaggs (*3613*) 1926.

Alterations in colonic function are well known to occur in human beings under stress and a recent report on this subject is that of Almy, Abbot, and Hinkle (*3602*) 1950. These authors made continuous kymographic records of the motility of the sigmoid colon in 18 patients suffering from "irritable colon." The symptoms tended to be worse during emotional conflicts. In general, it was found that a sudden reduction in tone and motility occurred when the patient's mood was one of inadequacy, self-reproach, and hopelessness. Often at such times weeping occurred.

It is known that stress produces an increase in the output of those urinary constitutents particularly representative of adrenal cortical activity. Associated with this response is a decrease in the eosinophile profile. Pincus in 1950 (*3609*) reported that responsiveness to stress may not be impaired in men surviving to old age without ill health or infirmity and that in these subjects the pituitary-adrenal mechanism involved in the response to acute stress may be relatively intact. Domanski, Swan, Wells, and Hughes (*3605*) 1951 have investigated the existence and character of the relationship between the eosinophile response and selected forms of exercise applied to normal human subjects with the aim of facilitating subsequent design of test stresses. The subjects were nine healthy males from 19 to 37 years of age. For the most part submaximal exercise was employed. This consisted of walking on a treadmill at a constant velocity of 3½ miles an hour with progressively increased elevation of the treadmill for 12 minutes or until attainment of a pulse rate of 180 per minute. Using the same technique, 6 subjects also walked to exhaustion. Exercise was not invariably associated with the negative eosinophile profile and the magnitude of the eosinophile response was different for different individuals. With exhaustive exercise in only 2 of 6 subjects was there any decrease in eosinophile profile as compared with exercise to a pulse of 180. In general, the rise in pulse rate followed a similar pattern in all 3 tests. Increase in duration of treadmill exercise accentuated the similarity, with pulse rate data for the exhaustion test being a near extension of the 180 pulse rate test findings. The exercise employed emerges as a relatively uncomplicated form of stress. Such stress of itself probably does not provoke a major emotional response.

In an attempt to use the urinary excretion of 17- and 20-ketosteroids as a measurement of stress, Stern (*3614*) 1949 measured the output of these substances during 6- or 7-hour flights. The output of 17-ketosteroids was increased on the average to an extent which could be judged to be just significant.

A somewhat similar study was carried out in 1950 by Cook and Wherry (*3603*). In this investigation the urinary 17-ketosteroid output of enlisted candidates for submarine service was measured during two stressful situations. One hundred and twenty subjects selected at random from the general group of enlisted candidates undergoing routine processing for submarine school were chosen. Two groups of 6 subjects each were tested during an intensive 3-day experimental period. The psychological stress situation consisted of administering the short group form of the Minnesota multiphasic personality inventory and the officers classification test. Finishing times were repeatedly stressed. The tank stress situation consisted of 2 escapes for each man from the training bell at 12 feet and 2 escapes from each of the 18- and 50-foot locks. Urine samples were taken on rising in the morning, 15 minutes before the stress, 15 minutes after the stress, and 2 hours after the stress ended. The output of androgens was positively related to the general level of 17-ketosteroid output and negatively related to age. The 17-ketosteroid output of subjects increased significantly over basal samples during both types of stressful situations. A greater output was evidenced during the tank stress than during the psychological stress situation. The amount of 17-ketosteroid increase during stress was considered by the authors a reliable measure of individual differences.

3602. Almy, T. P., F. K. Abbot, and L. E. Hinkle. Alternations in colonic function in man under stress. IV. Hypomotility of the sigmoid colon, and its relationship

to the mechanism of functional diarrhea. *Gastroenterology,* 1950, *15:* 95–103. *Abstr. World Med.,* 1950, *8:* 542.

3603. Cook, E. B. and R. J. Wherry. The urinary 17-ketosteroid output of naval submarine enlisted candidates during two stressful situations. *Hum. Biol.,* 1950, *22:* 104–124. [P]

3604. Darrow, C. W. and C. E. Henry. Psychophysiology of stress. pp. 417–439 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3605. Domanski, T. J., A. G. Swan, J. G. Wells, and L. B. Hughes. Physiological relationships in human stress response. I. Eosinophil response to muscular activity. USAF. Randolph Field, Texas. School of aviation medicine. *Project 21–32–025, Rept. no. 1,* October 1951, 13 pp.

3606. Grinker, R. R. and J. P. Spiegel. *Men under stress.* Blakiston. Philadelphia, 1945, 484 pp.

3607. Haggard, E. A. Psychological causes and results of stress. pp. 441–461 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3608. Landis, C. and R. Gullette. Studies of emotional reactions. III. Systolic blood pressure and inspiration-expiration ratios. *J. comp. Psychol.,* 1925, *5:* 221–252.

3609. Pincus, G. Measures of stress responsivity in younger and older men. *Psychosom. Med.,* 1950, *12:* 225–228.

3610. Selye, H. The general adaptation syndrome and the diseases of adaption. *J. clin. Endocr.,* 1946, *6:* 117–196. [R]

3611. Selye, H. *The physiology and pathology of exposure to stress.* Montreal, Acta Incorporated, 1950, 822 pp.

3612. Selye, H. *Annual report on stress.* Montreal, Acta, Incorporated, 1951, 644 pp.

3613. Skaggs, E. B. Changes in pulse, breathing and steadiness under conditions of startledness and excited expectancy. *J. comp. Psychol.,* 1926, *6:* 303–317. [P]

3614. Stern, M. I. The determination of urinary total neutral 17 and 20 ketosteroids in "Stress." Gt. Brit. FPRC. *F. P. R. C. rept. no. 719,* July 1949, 11 pp. [P]

3615. Vince, M. A. Learning and retention of an "unexpected" control-display relationship under stress conditions. Gt. Brit. MRC–APU. The psychological laboratory, Cambridge. *A. P. U. 125/50,* August 1950, 8 pp.

VI. FATIGUE

For general references on the subject of fatigue, papers by the following may be consulted: Ash (*3616*) 1914; Chapinis, Garner, and Morgan (*3622*) 1949; Katzell (*3627*) 1950; Laird (*3628*) 1948; Sayers (*3633*) 1942; and Smith (*3635*) 1916. Of these references the reports by Ash (*3616*) 1914 and Smith (*3635*) 1916 constitute early studies. The former is an excellent discussion of the general subject in both its somatic and psychological aspects. There is a good bibliography. Katzell (*3627*) 1950 has pointed out that fatigue is a complex psycho-physiological condition presenting at least three aspects: (1) a decline in the quantity and quality of production for a given amount of effort; (2) feelings of strain, irritation, and unpleasantness; and (3) a disturbed physiological state characterized by acceleration of catabolic processes and an accumulation of toxins and other chemical products of these catabolic processes. Changes in motivation also complicate the analysis and control of fatigue. Work decrement studies show that work output improves during the early stages of any segment of work. The production reaches a peak and later declines. As fatigue supervenes, effort may cause increased pulse rate, rise of blood pressure, alterations in differential white blood count, changes in blood sugar level, blood lactic acid level, oxygen consumption, etc. Although no precise physiological criteria of fatigue have been clearly established, measurements of physiological changes do reflect strain and have a value in attempting to identify work methods least taxing to workers. Feelings of strain usually develop earlier than decline in quantity and quality of production. Boredom is sometimes confused with fatigue but is to be differentiated from it in its subjective and objective characteristics. In boredom there is a desire for change rather than for rest. The work curve is irregular. Boredom may be relieved by variation of work methods, rotation of duties, and broadening the scope of the job. Fatigue may be reduced by steps to minimize its occurrence and provision for its dissolution after it appears. These steps include rest, shortening of long work periods, improving the pace of work, improving technique and equipment, controlling environmental factors such as noise, vibration, illumination, and atmospheric conditions, and improving personal factors such as clothing, rest and sleep habits, diet, drugs, and emotional state.

Sayers (*3633*) 1942 has pointed out that psychological and environmental factors are more important causes of fatigue than are physiological factors. He distinguishes 2 types of fatigue: (1) fatigue originating in the central nervous system and (2) fatigue originating partly in the central nervous system and partly in active muscles. Regarding the factor of effect on muscles in fatigue, the author considers that muscles are probably not injured directly by overwork under usual conditions.

Two papers on fatigue associated with visual performance may be consulted. The first of these by Simonson, Brozek, and Keys (*3634*) 1947 presents a laboratory study of visual fatigue. The second by Mackworth (*3631*) 1948 is a quantitative investigation of the breakdown of vigilance during prolonged visual search under laboratory conditions. The experimental situation was developed for the automatic presentation of occasional, brief, and barely visible signals throughout long watchkeeping

periods, the stimuli being given at irregular intervals. It was found that the efficiency of the subject during a 2-hour spell was definitely lower after the subject had been watching for about half an hour. During a 1-hour spell there was the same advantage in favor of the first half-hour. A half-hour rest period following a half-hour watch allowed a further one-half-hour spell with no detrimental effect on accuracy. Even a sudden, short telephone message in the middle of a 2-hour watch gave a temporary improvement.

Bast and co-workers have reported a series of experimental exhaustion due to lack of sleep and have examined the effects of such fatigue upon nerve cells in the spinal cord and medulla oblongata. In these studies, rabbits were prevented from going to sleep by being rotated in cylindrical cages. This rotation forced the animals to change their position about 8 times a minute. The animals were kept awake continually until exhaustion supervened. (Bast and Loevenhart (*3618*) 1927). Bast, Schacht, and Vanderkamp (*3619*) 1927 reported chromatolysis with vacuolation of the cytoplasm, particularly in the zone midway between the cell wall and the nucleus. Bast and Bloemendal (*3717*) 1927 found chromatolytic cells constantly in the reticular formation, and other nuclei of the medulla. The Nissl substance was granular and the cytoplasm was vacuolar. The nuclei of the cells were stained deeply but there was no migration of the nucleus. Cells of the hypoglossal nucleus showed no chromatolysis or other changes as a result of exhaustion by loss of sleep and this was true for all motor nerve cells supplying somatic musculature.

The fatigue of standing has been studied by Larsen (*3629*) 1948. In 17 observations on 12 healthy, young women the height of the center of gravity was lowered by an average of 0.216 percent of the body height as a result of 15 minutes of natural standing. In 21 observations on 17 similar young women, static effort produced a similar fall of 0.253 percent. It was suggested by the author that stance fatigue has its origin in excessive generation of nerve impulses brought about by repetitive stimulation of the antigravity musculature and by subacute cerebral hypoxia arising from the circulatory disturbance.

Circulatory changes are a part of the physiological pattern characteristic of fatigue. Leake, Grab, and Senn (*3630*) 1927 reported in rabbits fatigued to the point of collapse by deprivation of sleep that there was a fall in body temperature and a rise in pulse rate above normal followed by marked fall. There was a gradual fall in the respiratory rate. In studies reported by Bjerner (*3621*) 1950 normal human subjects responded to a reaction time test. Sleep deprivation was associated with poor performance and it was found that the poorest performance in the test, which usually occurred at 0400 to 0600, was associated with a transient fall in pulse rate as well as a depression of alpha activity of the electroencephalogram. In four out of the five subjects there was evidence of diurnal variation in the alpha frequency, the lowest rate coinciding with a tendency to a high percentage of error in responses to auditory stimuli. Hinrichs (*3623*) 1951 has reported hematological changes before and after fatiguing exercise in 87 athletes. Following the exercise there was a significant decrease in the percentage of polymorphonuclear leukocytes in 67 percent of the subjects and a significant increase in the percentage of lymphocytes in 70 percent. There was also a slight, but significant increase in the average number of nuclear lobes of the polymorphonuclear cells.

Watkins, Copp, Finesinger, Brazier, Shands, and Pincus (*3636*) 1948 conducted psychiatric and physiological studies of fatigue in psychoneurotic patients who complained of feelings of tiredness, weariness, or lassitude. Guilt and rejection situations precipitated fatigue episodes. Using a standard braking resistance on a bicycle ergometer for 3 minutes at 37 rotations per minute for men and 30 rotations per minute for women, the patients compared with normal controls showed significant increases in blood lactate and pyruvate, heart and ventilation rate, but no change in blood cholinesterase or in the electroencephalogram. A one-minute grip test on a spring dynamometer with tensions of 20 kg. for men and 15 kg. for women also gave significant increases in lactic acid production. Stimulation of the ulnar nerve for 4 minutes by unidirectional square wave impulses gave from 100 to 120 percent rise in blood lactate and pyruvate in both patients and controls, but no change in blood cholinesterase. Two-thirds of the patients reacted to stress situations by a drop in the lymphocyte count and an increase in uric acid in the urine, but not in the blood. The authors attributed this to an increased production of cortical steroids. According to Bast, Supernaw, Lieberman, and Munro (*3620*) 1928 exhaustion due to lack of sleep in animals resulted in vacuolation of the cytoplasm with pyknotic nuclei in the cells of the adrenal glands. Scattered patches of eosinophile cells were found in the adrenal cortical sinuses in 36 percent of the rabbits. There was marked congestion of the cortical sinuses and the vessels of the medulla with colloid-like material and cellular debris.

Ivy and Seashore (*3626*) have reported on the effects of analeptic drugs in relieving fatigue from prolonged military activity. A volunteer group of two officers and 14 men participated in 18 to 20 mile hikes with 20 pounds of equipment followed by all-night guard duty without relief. Caffein, benzedrine, and desoxyephedrine had measurable effects of relieving fatigue as demonstrated by various means including a visual flicker fusion test. Speed of visual discrimination reaction time was slightly, but reliably improved by all 3 drugs. Hand-arm sway was improved slightly by caffein and moderately by benzedrine and desoxyephedrine. Of all the 3 drugs the best all-round results were obtained from benzedrine. Caffein produced desirable subjective improvements but with little improvement in motor performance. Desoxyephedrine resulted in little change in subjective reports, but improvements in motor performance were as good as or slightly better than for benzedrine.

For further studies on fatigue, papers by the following authors should be consulted: Hollingworth (*3624*) 1914; Ishizuka (*3625*) 1951; Ota (*3632*) 1950; and Welford and Brown (*3637*) 1951.

3616. Ash, I. E. Fatigue and its effects upon control. *Arch. Psychol.*, 1914, *31:* 1–61. [D]

3617. Bast, T. H. and W. B. Bloemendal. Studies in experimental exhaustion due to lack of sleep. IV. Effect on the nerve cells in the medulla. *Amer. J. Physiol.*, 1927, *82:* 140–146. [P]

3618. Bast, T. H. and A. S. Loevenhart. Studies in exhaustion due to lack of sleep. I. Introduction and methods. *Amer. J. Physiol.*, 1927, *82:* 121–126. [P]

3619. Bast, T. H., F. Schacht, and H. Venderkamp. Studies in experimental exhaustion due to lack of sleep. III. Effect on the nerve cells of the spinal cord. *Amer. J. Physiol.*, 1927, *82:* 131–139. [P]

3620. Bast, T. H., Supernaw, J. S., B. Lieberman, and J. Munro. Studies in exhaustion due to lack of sleep. V. Effect on the thyroid and adrenal glands with special reference to mitochondria. *Amer. J. Physiol.*, 1928, *85:* 135–140.

3621. Bjerner, H. Alpha depression and lowered pulse rate during delayed actions in a serial reaction test. A study in sleep deprivation. *Acta physiol. scand.*, 1949, 19: 5–93. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology). 1950, *3:* 941.

3622. Chapanis, A., W. R. Garner, and C. T. Morgan. Working and resting. pp. 365–392 in: *Applied experimental psychology.* New York, John Wiley & Sons, Inc. 1949, 421 pp.

3623. Hinrichs, M. A. Further studies on some effects of physical fatigue on the peripheral circulation of athletes. *Res. Quart. Amer. Phys. Educ. Ass.*, 1950, *21:* 175–181. *Excerpta Medica.* Section II. (Physiology, Biochemistry, and Pharmacology), 1951, *4:* 768. Abstr.

3624. Hollingworth, H. L. Variations in efficiency during the working day.. *Psychol. Rev.*, 1914, *21:* 473–491.

3625. Ishizuka, T. On the relation between the fatigue; measured by flicker-test and the quantity of labour; counted by step-counter. *Osaka Univ. med. J.*, 1951, *3:* (Japanese text pagination) 217–222; (In Japanese with English summary) 217.

3626. Ivy, A. C. and R. H. Seashore. Effects of analeptic drugs in relieving fatigue from prolonged military activity. U. S. OSRD–NDRC. *O. E. M. cmr. 46, M. R. P. D. project 26,* no date, 4 pp. [P]

3627. Katzell, R. A. Fatigue and its alleviation. pp. 74–84 in: *Handbook of applied psychology. Volume I.* Edited by Douglas H. Fryer and Edwin R. Henry. New York, Rinehart and Company, Inc., 1950, ix, 380 pp. [R]

3628. Laird, D. A. Work and fatigue. pp. 738 (1)–738 (6) in *Oxford Medicine.* Volume I, Part II. Edited by H. A. Christian. New York, Oxford University Press, 1948.

3629. Larsen, E. M. The fatigue of standing. *Amer. J. Physiol.*, 1947, *150:* 109–121. *Excerpta Medica.* (Section II. Physiology, Biochemistry and Pharmacology), 1948, *1:* 182. Abstr.

3630. Leake, C., J. A. Grab, and M. J. Senn. Studies in exhaustion due to lack of sleep. II. Symptomatology in rabbits. *Amer. J. Physiol.*, 1927, *82:* 127–130. [M]

3631. Mackworth, N. H. The breakdown of vigilance during prolonged visual search. *Quart. J. exp. Psychol.*, 1948, *1:* 6–21.

3632. Ota, H. On the changes of nervous function in fatigue. *Hukuoka Acta med.*, 1950, *41 (6):* (English text pagination) 63. (In Japanese with English summary).

3633. Sayers, R. R. Major studies of fatigue. *War Med., Chicago*, 1942, *2:* 786–823.

3634. Simonson, E., J. Brozek, and A. Keys. Visual fatigue. *Fed. Proc. Amer. exp. Biol.*, 1947, *6:* 202.

3635. Smith, M. A contribution to the study of fatigue. *Brit. J. Psychol.*, 1916, *8:* 327–350.

3636. Watkins, A. L., S. Cobb, J. E. Finesinger, M. A. B. Brazier, H. C. Shands, and G. Pincus. Psychiatric and physiologic studies on fatigue. Preliminary report. *Arch. phys. Med.*, 1947, *28:* 199–206. *Excerpta Medica.* (Section II. Physiology, Biochemistry and Pharmacology), 1948, *1:* 183. Abstr.

3637. Welford, A. T. and R. A. Brown. Two experiments on fatigue as affecting skilled performance in civilian air crew. *Brit. J. Psychol.*, 1950, *40:* 195–211. *Excerpta Medica.* (Section II. Physiology, Biochemistry, and Pharmacology), 1951, *4:* 840.

VII. MORALE

It has been universal experience that good morale in a competent group is essential to fighting effectiveness. However, it is not easy to define exactly the components which make for good or bad morale or to say precisely what are the factors valuable in maintaining morale. The latter question has been discussed by Bassan (*3638*) 1947. This report tells of conditions existing aboard "The Sullivan" during 12 months of active war operation in the Pacific area and shows how care and foresight made a happy ship with no morale breakdown during the period. The men received long and careful indoctrination training during the fitting out and shakedown period. Each cruise lasted about 30 days during which time the crew was divided into three sections. Each section stood the same watch during the cruise. They could thus become familiar with

their routine. Care was given to planning tasty meals and the men were told of their mission and destination and felt their part and responsibility in the operation. News was given the men as soon as possible and they were provided with music, books, movies, and whenever possible, athletic sports. Shore parties were made possible whenever conditions permitted. Medical care was provided as needed. The author considered none of the factors mentioned could be thought of singly as the thing that kept the men going. Above and beyond any one single factor, there was an intangible element that seemed to produce harmonious interpersonal relationships between the officers themselves, the officers and men, and among the men themselves.

Leadership appears to be one of the significant factors in morale. French has discussed this in a paper (*3639*) published in 1949. He discusses various methods of appraising morale or group effectiveness, involving use of questionnaires, observation and interview methods, sociometric procedures, projective techniques, group indices, and situation tests. The author considers it a pertinent question as to whether a group functions better if it is composed of individuals of similar or dissimilar characteristics. He states that mutual selection of members often works for better adjustment of the group. Satisfaction with job assignment is considered perhaps the single most important factor in morale. Length of time spent in an assignment or locality is often important. Since the manipulation of variables related to morale is primarily the responsibility of appointed leaders, the factor of leadership assumes central significance in the quality of morale. A large share of research on this problem of leadership and morale has been dominated by the concept of leadership as a personality trait in the leader. A newer concept now developing views leadership as a process of interaction between individuals in which the characteristics of the leader are important only in relation to the situation, that is to say, the goals and other characteristics of the group and relevant external circumstances. The author considers intensive analysis of leader-follower interaction essential to intelligent research in selection and training of leaders.

Insight into problems of morale and leadership in German submarines has been given by Lueth (*3640*) 1947. This author considers that morale of the crew depends upon discipline, success of operation, well organized daily routine, example and correct attitude of officers, and real spiritual leadership for the men together with a genuine concern for their personal welfare. In this paper a description is given of various procedures instituted for the comfort of the crew, including music, books, etc. It appears that the discipline was stern with authoritarian control over even quite minute elements of personal conduct.

With new and more rigorous conditions of operation inevitably to be imposed by modern warfare and new type submarines it is imperative that the problem of morale be constantly reevaluated. It is likely in the future that good morale will play an even more important part than in the past in the success of patrols.

3638. Bassan, M. E. Some factors found valuable in maintaining morale on a small combatant ship. *Bull. Menninger Clin.*, 1947, *11:* 33–42.

3639. French, R. L. Morale and leadership. pp. 463–488 in: *A survey report on human factors in undersea warfare.* Washington, D. C., National Research Council, 1949, 541 pp.

3640. Lueth, W. Problems of leadership in a submarine. A lecture by a German submarine commander, 17 December 1943. U. S. Navy. ONI. *Rept. no. 11746,* 1947, 15 pp.

VIII. SLEEP-WAKEFULNESS

For papers on the general subject of sleep, reports by the following authors should be consulted: Bartley and Chute (*3646*) 1947; Endres and von Frey (*3651*) 1930; Gillespie (*3656*) 1929; Hess (*3658*) 1949; Johnson and Swan (*3662*) 1930; Kayser (*3663*) 1949; Pieron (*3685*) 1913; and Ranson (*3687*) 1934.

Much has been written on the mechanisms of sleep. The following significant references to theories of sleep should be consulted: Atkinson (*3642* and *3643*) 1947; Drogendijk (*3649*) 1949; Ivy and Schnedorf (*3661*) 1937; Learoyd (*3677*) 1950; Pavlov (*3683 and 3684*) 1927; Singh and Singh (*3694*) 1946; and Stern, Marijan, and Eisen (*3696*) 1950. Sleep is envisiged as a process of internal inhibition (*3683, 3684,* and *3694*). It is governed by the central nervous system and both the cortical and sub-cortical mechanisms are involved in the process (*3642* and *3643*). The source of the central nervous inhibition may be a chemical substance—a "fatigue fluid" or "hypnotoxin" (*3649* and *3661*). Stern, Marija, and Eisen (*3696*) 1950 have reported experimental studies on the role of calcium in the activation of the cholinergic system during sleep. Animals treated with hypnotic doses of medinal after calcium had been removed with sodium oxalate fell asleep after a longer interval than controls. Rats and rabbits in which calcium had been removed by sodium oxalate showed a decreased cholinesterase activity in the hypothalamus while the cholinesterase in the cortex did not change. Additional small amounts of calcium chloride restored the cholinesterase activity to almost normal rate.

Clinical as well as experimental investigations of cerebral localization of the sleep mechanism have implicated various nuclei in the diencephalon and mesencephalon as well as higher centers. Papers by the following may be consulted on this subject: von Economo (*3650*) 1930; Harrison (*3657*) 1940; Manceau and Jorda (*3678*) 1948; Ranström (*3688*) 1947; Rowe (*3692*) 1935; and Serota (*3693*) 1939. According to von Economo (*3650*) 1930 the sleep center has its location in the area of the brain affected by encephalitis lethargica. Von Economo conceived that the virus of encephalitis has an affinity for the sleep center and that the action of sleep-regulating center probably consists in a coordination of the changes in vegetative and psychic functions which occur in sleep. According to von Economo, normal sleep may be considered as an inhibitory action brought about by the center of sleep regulation acting upon the cerebral cortex and thalamus. Circulating toxins may set the sleep center into action.

Rowe (*3692*) 1935 concluded from a survey of the literature that evidence favoring localization of the sleep mechanism in the diencephalon is inconclusive and not entirely satisfactory. On the basis of cases studies he suggested that disturbances of sleep result from lesions of a rather diffuse, central correlating mechanism involving the thalamus, hypothalamus, and mesencephalon. A correlation between hypothalamic activity and sleeping and waking states has been experimentally determined in cats by Serota (*3693*) 1939. This author found by direct measurements that the hypothalamus was warmer than the cortex. This was true in unconscious, anesthetized animals and it was found that the absolute temperature fluctuated during the waking state, sometimes in a rhythmic manner. The positive temperature difference between the hypothalamus and the cortex was found to increase in an irregular fashion with activity. Emotional state, such as fear, rage, or anticipation of food, increased the relative temperature of the hypothalamus. Sleep decreased the hypothalamic temperature and stabilized it. On awakening, the hypothalamic temperature rose earlier and higher than that of the cortex, caudate nucleus of Ammon's horn. The specific temperature decrease of the hypothalamus in sleep was shown to be due to lowered cell metabolism rather than to a marked change in hypothalamic blood flow. This indicated to the author that sleep is associated with decreased rather than increased activity of the hypothalamic sleep center.

An attempt to produce sleep by diencephalic stimulation was reported by Harrison (*3657*) in 1940. This author applied destructive and stimulating electric currents to the hypothalamus, thalamus, head of the caudate nucleus, septum pellucidum, and the region of the anterior commissure in waking cats. Somnolence was produced by destructive action of currents when applied to the lateral hypothalamic area. Catalepsy tended to develop when lesions involved the medial and posterior part of the hypothalamus. Somnolence was produced by destructive electric currents applied to the lateral group of thalamic nuclei, but the strength and duration of these currents was much greater than in the hypothalamic experiments. Extensive lesions of the head of the caudate nucleus did not produce somnolence. The author considers that his experiments offer no evidence to support the theory that sleep is a phenomenon of active inhibition.

In a report published in 1947, Ranström (*3688*) points out that the literature on the physiology and pathology of sleep infers that the regulation set up for sleep-wakefulness must exist within the posterior part of the hypothalamus. In the author's experiments, electrolytic lesions placed by an X-ray stereotaxic method within the posterior part of the hypothalamus of cats produced sleep of some days duration. The period of sleep set in after an interval of some hours following the operation and not immediately after placing the lesion. The sleep effect was presumably brought about by substances liberated by necrosis. The author considers that these are not nonspecific products of necrosis but substances which occur performed in this part of the brain. Lesions in the posterior part of the hypothalamus of rabbits brought about no sleep effects and it was presumed that rabbits lack a regulatory center for sleep in this area. Histological characteristics of neurones in the hypothalamic region suggested to the author that cells of this part of the brain are capable of secretory function. Sleepiness produced experimentally by electrolytic lesions in the hypothalamus was considered to be brought about by liberation of hormonal substances from the neurones themselves.

A number of papers have been written on the physiological and biochemical changes occurring during sleep. Richter and Dawson (*3690*) 1948 found that the lactic acid content of the rat brain was reduced in sleep and increased in emotional excitement. The rise in lactic acid content in the brain during emotion was not due to concomitant muscular activity since the effect was still observed in animals immobilized by d-tubocurarine. The onset and termination of sleep is not accompanied by significant change in blood flow through the brain according to Gibbs, Gibbs, and Lennoux

(*3655*) 1935. According to Barker and Burgwin (*3645*) 1950 much misunderstanding is produced by trying to identify the hypnotic state with sleep. The hypnotic trance leaves the alpha rhythm unchanged except for short periods following suggestions or instructions. However, when true sleep is induced by hypnosis the sleep patterns are those observed as in natural sleep. Euziere, Passouant-Fontaine, Passouant, and Latour (*3652*) 1950 have carried out electrocardiographic studies of spontaneous sleep and sleep provoked by pentothal in neurological patients. On the basis of 30 tracings of spontaneous sleep and 70 tracings of sleep produced by pentothal obtained from patients with encephalitis, epilepsy, cerebral atrophy, and tumours, it was concluded that in diffuse brain lesions there is a decrease in the number of transitory stages between sleep and wakefulness. In localized brain lesions there is a dissimilarity in the EEG tracings from different regions. In epilepsy characteristic bursts may appear in wakefulness, normal sleep, induced sleep, and semi-sleep, but particularly in the frontal region. According to the authors the frontal lobe may be the last link between the cortex and the subcortical regions to disappear during sleep and the first to reappear as a result of external stimulation. Regarding the effect of sleep on cerebrospinal fluid circulation, Gans (*3654*) 1950 has offered the hypothesis that sleep influences the flow of the cerebrospinal fluid so that it passes from the ventricles to the subarachnoid spaces entirely or partly by a transcerebral route, bringing nourishment to, and removing waste products from the brain cells. For studies on the effects of sleep on metabolism papers by the following may be consulted: Banche (*3644*) 1950; Collip (*3647*) 1920; Frommel, Beck, Favre, and Vallette (*3653*) 1947; and Mason and Benedict (*3679*) 1934.

Research on the physiology of sleep and sleep rhythms is associated with the name of Kleitman and his colleagues (*3648, 3665, 3666, 3667, 3668, 3669, 3670, 3671, 3672, 3673, 3674,* and *3675*). Kleitman (*3665*) 1923 reported on the effects of prolonged wakefulness on man. More phosphorus was said to be excreted in the urine per hour during sleep than during wakefulness, independently of the volume of urine secreted (*3666*). It was suggested that this increase in the excretion of phosphorus during sleep is due to more complete muscular relaxation in that state. Kleitman and Camille (*3671*) 1932 reported that decorticated dogs have several periods of sleep alternating with periods of activity each 24 hours. The activity consisted of almost incessant walking in circles. Most constantly occurring period of sleep followed shortly upon feeding. It was concluded that diurnal sleep in dogs depends for its establishment and persistence upon the integrity of the cerebral cortex. According to Kleitman and Doktorsky (*3672*) 1933 assumption of horizontal position generally leads to a fall in body temperature. Onset of sleep tends to accentuate the downward trend of temperature preceding sleep. Awakening is not characteristically followed by change in body temperature. According to Cooperman, Mullin, and Kleitman (*3648*) 1934 sleep following 60-hour periods of wakefulness is characterized by decrease in the frequency of movements, in time spent in stirring, and in the total number of movements.

For studies on the sleep-wakefulness cycle, 3 particular papers by Kleitman should be consulted (*3668, 3669,* and *3670*). The latter report concerns the sleep-wakefulness cycle of submarine personnel. Although there is nothing physiologically compelling about the 24-hour alternation of sleep and wakefulness, according to the author, the cycle stems from the fact of the succession of day and night and community life is adapted to this. A simple test of the degree of adaptation of the individual to this cycle is the fixity of the diurnal body temperature curve which may, however, be changed by following a new schedule of activities for a length of time. Efficiency of performance and degree of alertness during the waking phase of the cycle are seen by the author to conform to the rise and fall of body temperature. On awakening, the temperature is about the same as at retiring and performance is very similar. Both temperature and performance level rise and reach a peak or plateau in the early afternoon. Later on, sometime in the evening, the body temperature turns downward and at the same time there is a progressive decline in efficiency of performance. The author carried out studies of the sleep-wakefulness cycle on the U. S. S. *Dogfish* carrying 8 officers and 66 men aboard. The mean age of the officers and crews was 25 years. Some had been on submarines as long as 14 years. Hours of watches were fixed for the entire cruise with meal hours coinciding with watch changes. According to the schedule someone was asleep at all times and the total duration of sleep per 24-hour period averaged 8½ hours per man. This was obtained usually in 2 or 3 periods. There was a tendency for wakefulness to be concentrated during the afternoon and evening. Temperature recording on 9 subjects showed that it was possible while isolated in a submarine to preserve the shore type of 24-hour body temperature curve by following a customary routine of living. It was also possible to establish 2 equal 12-hour curves on a 4 hours on and 8 hours off

watch schedule. It was considered that personnel overestimated their ability to become fully alert on short notice. Both the narrowness of the bunks and their vertical crowding discouraged frequent changes in sleeping posture essential for restful sleep. Very few subjects complained of their bunks and most considered them but little less adequate than on shore stations. In the new schedule of watches, the most revolutionary feature was the necessity for preparation of 9 meals a day. Trial runs showed that cheerful acceptance of the new schedule by the crew would be a necessary prerequisite before such could be adopted.

A report by Husband (*3660*) 1935 indicates that there is no significant difference between the value of continuous and interrupted sleep. In Husband's experiments a subject slept for 8 consecutive hours nightly for one month while during the second month he slept 3 hours, remained awake 3 hours and then slept 3 hours more. Various performance tests indicated no change in efficiency of the subject during the total time of the study.

For studies on the effects of loss of sleep, papers by the following may be consulted: Laslett (*3676*) 1924; Rakestra and Whittier (*3686*) 1923–24; Robinson and Herrmann (*3691*) 1922; and Weiskotten (*3697*) 1925. For studies on the effects of hypoxia and drugs upon sleep papers by the following may be consulted: Smith (*3695*) 1946; Mullin, Kleitman, and Cooperman (*3680*) 1933; and Hollingworth (*3659*) 1912. Other references on sleep are given as follows: Andreyeff (*3641*) 1951; King (*3664*) 1946; Page (*3682*) 1935; and Reed and Kleitman (*3689*) 1926.

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IX. DUTY AND REST PERIODS

Most civilian enterprises employ the majority of their personnel between the hours of 0800 and 1800 and the daily routine of these employees and their families is built around these conventional working hours. Since operation of a ship under way requires a round-the-clock schedule of activities, the crews work under a rotation of watches which usually involves a "4 hours on and 8 hours off" routine. This type of watch schedule places some duty sections at a disadvantage with respect to meals and recreation, as well as sleep. Apart from this, during general quarters all hands must be at their battle stations. Some of the stress brought on by odd watch hours is lessened by "dogging" the watch: viz the 2000 to 2400 watch is split in two, with the new section going on watch at 2200. This type of watch scheduling may appear to be fair to all hands but it probably wreaks havoc with the normal diurnal cycle of sleep and wakefulness. It is probably true that efficiency is lowered during the hours of darkness when the body temperature is low and these are important hours to a fighting ship since opportunities for enemy attack are at a maximum.

Normally aboard the operating submarine there are three watch sections. Section I (2 officers and 16 men) has the 0400 to 0800 and 1600 to 2000 watches; Section II (2 officers and 18 men), the 0800 to 1200 and 2000 to 2400 watches; Section III (2 officers and 17 men), the 0 to 0400 and 1200 to 1600 watches. Personnel of Section IV (2 officers and 15 men) are not required to stand watches, but either followed a frankly shore-type schedule of activities (cooks and messmen) or are on call at all hours. The hours of watches are fixed for the entire cruise (except for the officers), and the meal hours are made to coincide with watch changes—

breakfast at 0730 to 0800, dinner at 1130 to 1200 and supper at 1930 to 2000.

Pioneer work in the revision of the older standard watch schedules has been carried out by Kleitman and the report by Kleitman and Jackson (*3700*) 1950 describes and evaluates a schedule which permitted the continuance of a normal diurnal temperature cycle. The two-fold purpose of this study was to determine the ease with which naval personnel adapted themselves to various watch schedules as judged by their diurnal body temperature curves, and to discover the existence, if any, of a correlation between body temperature and alertness, as indicated by performance in several tests and in other aspects of behavior. Results obtained indicated a variability in adjustment. On the rotating (dogged) schedule of watches the pattern of the diurnal body temperature changes was the same as on shore. Color naming, and to a lesser extent, reaction time and Link trainer performance, showed a diurnal variation particularly on the dogged watch routine, the only one which permitted testing around the clock. In general, the higher the body temperature the better was the performance.

Operationally, the original Kleitman schedule has proven to be impractical because of its requirement of 9 meal servings each day. Aside from this, the duration and distribution of on-and-off watch periods are not equal for all sections.

Another watch schedule was tried and tested physiologically and psychologically at sea by Utterback and Ludwig (*3702*) 1949. This schedule requires 3 watches of 3, 3, and 2 hour durations by each section of the crew, and provides a continuous period off duty of 10 to 12 hours. These studies were made on 3½, 4, 19, and 21 day cruises aboard the U. S. S. *Tusk,* U. S. S. *Sirago,* and U. S. S. *Cubera.* The schedule was compared with the present system of 4-hour watches separated by 8 hours off. The rapidity with which the men adapted to the schedule was determined by means of oral temperature cycles, which also afforded an indication of the alertness and efficiency of men on watch. On the basis of body temperature studies, the proposed schedule was found to be a definite improvement over the present one. The advantages accrued were similar to those found by Kleitman. An extra advantage was the requirement of only 4 meals for a 24-hour period, each section receiving 3 meals per day. As with the Kleitman watch bill, the duration and distribution of on-and-off watch periods were not uniform for all sections.

The adjustment of watch schedules to match body temperatures and the attempt to alter temperature curves to fit an unusual routine are based upon information obtained from normal sleep-wakefulness cycles and efficiency measurements correlated with body temperature. A more complete review of the physiological process of sleep and sleep-wakefulness cycles is provided in section on sleep-wakefulness (p. 321).

Studies by Kleitman and Engelmann (*3699*) in 1947 on the activity of rabbits as related to body temperature showed that with continuous access to food, activity was lowest during daytime hours when the rectal temperature was low. When food was available only from 9–10 a. m. to 3–4 p. m., activity became decidedly monophasic, increasing sharply in the morning, prior to the time of feeding and continuing at a high level during the day. The rectal temperature showed a marked rise during the feeding period, reaching its high level in the afternoon, instead of late in the evening. Although usually considered polyphasic, rabbits under ordinary laboratory conditions show a distinct 24-hour cycle of activity and body temperature. The tendency to a night-time high, when access to food was continuous, could easily be modified by making food available for only a few hours during the day. Earlier experiments by Kleitman, Titelbaum, and Feiveson (*3701*) 1938 on the effects of body temperature on reaction times in man showed that the best performance was obtained in the afternoon with poorer performance records during the morning hours. This variation appeared to be dependent upon the diurnal body temperature. A spontaneous or induced change in body temperature was reflected in a change in the opposite direction of reaction time.

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X. PSYCHIATRIC BREAKDOWN

The situational stresses of submarine war patrols during World War II were often extremely trying. The experiences of some of these patrols have been summarized by Duff and Shilling (*3704*) 1947. Depth charging, heat, and other environmental stresses took their toll and sometimes taxed beyond the limits the endurance of the crews. One account describes a terrific explosion within a submarine. All hands not holding onto something were knocked from their feet. Thick toxic smoke filled the maneuvering room and the after torpedo rooms. All hands were violently ill. Another account tells of the intolerable conditions imposed by heat and humidity. In one case the maneuvering room temperature was 125° F. All hands were stripped down to their shorts and shoes were removed. Men perspired so profusely that in an hour or more the decks were slippery with sweat. Towels used to keep perspiration out of the eyes became wringing wet; socks could be wrung out like rags. Everyone drank large quantities of water and took salt and aspirin tablets. As time went by the air became so oppressive and stifling that it was difficult to breathe. Headaches were prevalent and severe. It was impossible to sleep.

On many patrols heat rash caused serious discomfort. The enervation from the heat became so striking that physical exertion such as required to change and maintain depth control would exhaust a planeman. Controllermen had to be spelled frequently. Efficiency and reaction times were strikingly reduced. Errors were prevalent, even among experienced men. There was an increase in accident rate. Tempers were short. Nerves were on edge. Sometimes, apathy developed. As the younger crewmen folded up, older and more phlegmatic men would take over. Some without permission, others after requesting relief would quietly shove off and lie down on the cooler spots of decking. Sometimes, two men would take turns, the off watchman resting on the deck beside his station. Generally, there was no evidence of hysteria, the men carrying out their duty to the limit of physical and mental endurance. Oftentimes, upon surfacing there was distressing nausea and vomiting. Under such conditions, submarines were no longer in a position to fight or defend themselves. Though the more serious of these symptoms passed off quickly with rest and fresh air, the men were often fatigued and extremely tense for days thereafter.

These brief pictures, which by no means represent the most dangerous or stressing experiences of submarine crewmen, afford insight into the severity of submarine operations. It is remarkable that under conditions often similar to and exceeding these there were only approximately 56 psychiatric casualties out of a total of 126,160 man-patrols during World War II. Duff and Shilling have analyzed the possible reasons for such remarkable performance. These include sound selection techniques, training, morale, medical care, rest camps, rotation of duty, and confidence in officers. Psychiatric casualties in submarine warfare have also been discussed by Duff and Shilling in another publication (*3703*) 1947.

It was not uncommon in the 24-hour period following a depth charge attack to see a number of cases of mild gastric disturbance with nausea, abdominal cramps, diarrhea, indigestion, and headaches usually with rapid recovery without treatment (*3709*). Occasionally the entire crew exhibited generalized impairment of appetite after a depth-charge attack. Symptoms also included anxiety, dizziness, and insomnia. These occurred not only in inexperienced personnel, but also in veteran submariners.

Psychiatric reactions developing in operators of antisubmarine sound gear have been described by Will (*3710*) 1945. Case histories are given of 2 sound operators who developed acute schizophrenic episodes while at sea. The author emphasized the importance of careful preselection of men for these duties and more frequent rotation of the watch with additional brief rest periods.

For 16 months during 1943 and 1944 McHarg (*3707*) 1946 had the opportunity of studying psychiatric disabilities in submariners of the British submarine service in a home-based submarine flotilla. One-half of the cases seen were referred to neuropsychiatric specialists and one-third eventually became permanently unfit for submarine duty. The rate of admission to hospital was less than one percent per annum. The rate of invaliding from the Navy on psychiatric grounds was less than 0.3 percent. This study of 71 cases undertaken by the author was carried out to verify the impression that the incidence of serious psychiatric illness among submariners is very small. Stress plays a large part in the majority of cases. Indications are that submariners are stable individuals. Less stable men do not reach the submarine service or are eliminated in early stressful situations.

Several case histories of submariners with nervous symptoms have been reported by Essen (*3705*) 1948. This paper is of particular importance since the submariners in question were members of the German submarine service. The author has described psychosomatic and other symptoms of

patients entering the clinic with symptoms of fatigue and nervous exhaustion.

The remarkably low incidence of psychiatric breakdowns in the U. S. submarine service in World War II does not justify complacency as to the importance of the psychiatric problems or the potential hazards in the future. It becomes increasingly essential to eliminate the psychiatrically unstable in the early stages and to improve techniques for the recognition of those candidates for submarine training who are likely to become psychiatric casualties. The selection program developed during World War II undoubtedly was effective in eliminating most of the unfit. For example, the low incidence of claustrophobic fears among submariners is undoubtedly due to the fact that many applicants with serious personality defects were eliminated by the selection procedures, not the least important of which was the escape training tank program (*3706* and *3708*).

3703. Duff, I. F. and C. W. Shilling. Psychiatric casualties in submarine warfare. pp. 183–198 in: *History of submarine medicine in World War II.* Edited by C. W. Shilling and J. W. Kohl. U. S. Navy. Submarine base, New London, Conn. Medical research laboratory, 25 May 1947, 328 pp.

3704. Duff, I. F. and C. W. Shilling. Psychiatric casualties in submarine warfare. *Amer. J. Psychiat.,* 1947, *103:* 607–613.

3705. Essen, K. W. The nervous syndrone of submariners. Clinical findings, pathogenesis, attempt at therapy. pp. D IV–1—D IV–40 in: *Monograph on submarine medicine, Folio VII,* Germany. U. S. Zone. Office of naval advisor. 1948. [R] [CH]

3706. Lewin, B. D. Claustrophobia. *Psychoanal. Quart.,* 1935, *4:* 227–233.

3707. McHarg, J. F. The mental health of submariners, with special reference to 71 cases examined psychiatrically. *J. Ment. Sci.,* 1946, *92:* 343–356.

3708. Schmideberg, M. A note on claustrophobia. *Psychoanal. Rev.,* 1948, *35:* 309–311.

3709. U. S. Navy. BuNavPers. (C) Psychiatric casualties in submarine warfare. pp. 150–155 in: *Submarine medicine practice. NavPers 10838,* March 1949, 182 pp. [D] [CH]

3710. Will, O. A., Jr. Certain psychiatric reactions in operators of antisubmarine sound gear. Report of two cases. *Nav. med. Bull., Wash.,* 1945, *44:* 746–748.

Special Problems of Swim-Diving

I. GENERAL STUDIES

World War II and the years following have seen an increasing awareness of the military potentialities of individual men swimming, "skin-diving," or using self-contained diving equipment independent of connections to the surface. The advantages of freedom of movement and of stealth fit such men for a variety of tasks which can be accomplished by other means only with great difficulty, if at all. Their accomplishments have included penetration of harbor defenses and sinking large warships, reconnaissance of beachheads, clearing of underwater obstacles before and after assaults, and location and disposal of mines. Self-contained apparatus has advantages in certain operations where conventional diving gear is generally used but where lifeline and airhose may be more of an encumbrance than a safeguard, where heavy surface equipment is a handicap, or where conventional mooring and other time-consuming preparations are impractical.

In addition to increasing military and commercial applications, this form of diving has gained widespread recreational use in spear fishing and underwater "sightseeing." It has also become a recognized scientific technique in marine biology, oceanography, and submarine archeology. These developments strongly suggest that what may be called "swim-diving" will have continuously increasing importance in underwater work. Since it involves problems peculiar to itself in addition to those associated with conventional diving and swimming, and since these peculiar problems have received only a fraction of the attention they deserve, it is to be hoped that the next few years will see many new studies on this subject.

In discussing equipment for underwater warfare in World War II, Davis (*3713*) 1951 provides information not only on breathing apparatus and midget submersible craft, but also about a variety of applications of such apparatus. These include the "human minesweepers" and "human torpedoes," and the history and work of "frogmen." Excellent references are included. Waldron and Gleeson (*3722*) 1950, give an exciting account of the background and development of "frogmen" techniques, beginning with the operations of Italian divers who rode two-man torpedoes and successfully damaged several large warships by attaching limpet mines. Subsequently, the British adopted the idea and solved many engineering and research problems involved in such operations. The Normandy invasion was greatly facilitated by port clearance parties which gave individual attention to enemy mines. The partial destruction of the celebrated Remagen bridge appears to be the only notable achievement by the Germans in this type of activity.

The United States Navy Underwater Demolition Teams (U. D. T.) had their beginning in 1943. Robb (*3719*) 1951 describes the costly lesson learned at Tarawa concerning their potential value. It was such lessons that greatly stimulated U. D. T. development. Subsequent operations and the techniques employed, mainly without the use of breathing apparatus, are described. An account of the U. D. T. techniques of screening applicants provides a graphic illustration of the gruelling physical and mental stresses imposed upon trainees: "For 6 days and nights of 'hell week' the trainees are subjected to every trial of stamina and nerves their resourceful instructor can devise * * * early morning swims, each progressively longer, are made in overcoat weather. As late as early December, trainees take daily swims in the Atlantic wearing only swim trunks." Lambertsen (*3718*) 1947, who developed a closed-circuit oxygen unit and participated in the training and operations of the U. S. Office of Strategic Services' "operational swimmers," reports on the problems which arose during more than 5,000 man-hours of underwater swimming with the equipment. Medical problems encountered by an underwater demolition team are discussed by Waite (*3721*) 1951.

Dugan (*3715*) 1948 discusses the "diving lung" developed by Cousteau and Gagnon for the French navy. With this equipment, an open-circuit compressed air unit, Cousteau was able to reach a depth of 210 feet; and dives to 100 feet without connections to the surface became commonplace. Divers

using this equipment were observed medically for several years without detecting any pulmonary, circulatory, or auditory changes. Details of training and requirements for this type of work in the Italian navy as of 1942 are included in its manual for shallow water divers (*3717*).

Schenk and Kendall (*3720*) 1950 provide a popularized approach to the construction and operation of shallow-water and self-contained equipment. Wartime underwater research activities of the Canadian navy, including some of interest in "swim-diving," are reported by Delorme and Locke (*3714*) 1944. Further information on diving with open-circuit gear is incorporated in a text on diving by Tailliez, Dumas, Cousteau, Alinat, and Devilla (*3802*) 1949.

3711. Akashi, K. Morphological study of AMA (women divers). Part I. Morphology of the chest. *Folia endocrin. japon.,* 1951, *27 (4)*: (English text pagination) 121–122. (In Japanese with English summary).

3712. Akashi, K. Morphological study of the AMA (women divers). Part II. Morphology of the lower torso. *Folia endocrin. japon.,* 1951, *27 (4)*: (English text pagination) 123–124. (In Japanese with English summary).

3713. Davis, Robert H. Diving equipment for underwater warfare in the second World War. pp. 290–324 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., Fifth edition, 1951, 670 pp. [D]

3714. Delorme, E. J. and W. Locke. Report on the medical aspects of diving practice of interest to the Royal Canadian Navy. (Summary of report). Canada. NRC. Proceedings of the third meeting of the Associate committee on naval medical research. *Appendix R, Report no. C4080,* 15 May 1944, 6 pp.

3715. Dugan, J. The first of the menfish. *Sci. Ill.,* 1948, *3: No. 12:* 30–32, 68–69.

3716. Gay-French, S. Oto-rhinological problems of offensive diving. *J. Laryng.,* 1946, *61:* 417–440.

3717. Italian Royal Navy. [Royal Navy manual for shallow water divers.] Underwater department of the Royal Navy, Divers School, 1942, 47 pp.

3718. Lambertsen, C. J. Problems of shallow water diving. *Occup. Med.,* 1947, *3:* 230–245.

3719. Robb, J. E. UDT pays off. *Milit. Rev. Fort Leavenw.,* 1951, *13:* 3–14.

3720. Schenk, H., Jr. and H. Kendall. *Shallow water diving for pleasure and profit.* Cambridge, Maryland, Cornell maritime press, 1950, 138 pp.

3721. Waite, C. L. Medical problems of an underwater demolition team. *U. S. Armed Forces med. J.,* 1951, *2:* 1317–1326.

3722. Waldron, T. J. and James Gleeson. *The frogmen. The story of the wartime operators.* London, Evans Brothers Limited. 1950, 191 pp.

II. PHYSIOLOGICAL PROBLEMS OF SWIMMING AND SWIM-DIVING

Many problems encountered in conventional diving have already been discussed in foregoing sections. These include such topics as the physiological effects of elevated atmospheric pressures (p 7), decompression sickness (p. 159), ear, nose, and throat disturbances (p. 151), oxygen intoxication (p. 182), anoxia (p. 17), carbon dioxide toxicity (p. 54), "squeeze" (p. 257), air embolism (p. 255), immersion in cold water (p. 112), and underwater blast (p. 258). Physiologically, a man is diving when he exposes himself to the underwater environment, regardless of his method. Hence, all of these discussions concern swimming and the use of self-contained apparatus, although in some cases with unusual application or emphasis.

Studies primarily concerned with surface swimming have been included in this section, not only for their potential significance in swim-diving but because swimming itself has achieved a measure of military importance. As has been pointed out, swim-diving involves not only factors which are common to all types of underwater work and those related primarily to swimming but also a number of problems which are essentially different. These unique problems constitute a major area of needed study. A review of some of the principal difficulties encountered in swim-diving is provided by Lambertsen (*3718*) 1947.

Several of the problems most peculiar to swim-diving arise from the fact that the diver, who lacks a helmet and partially inflated suit, is exposed not only to the hydrostatic pressure at a given depth but also to the different pressures of the various depths subtended by his body and equipment. While these differences in hydrostatic pressure are small when compared to the total pressure, they assume significance in a delicately balanced mechanism such as that of respiration, where pressure differences of a few centimeters of water are important. The hydrostatic pressure of water acts upon the thoracic cage, tending to produce a certain pressure therein. It also acts upon any exposed, nonrigid portion of his breathing apparatus such as a rebreathing bag or demand valve. If these pressures are not essentially balanced, the mechanical work of breathing may be greatly increased with consequent respiratory fatigue. There is also a possibility of secondary circulatory impairment and actual pulmonary damage. The implications of such imbalances can best be appreciated by referring to studies on the mechanics of breathing and the effects of breathing resistance such as those of Fenn (*3726a*) 1951 and Cain and Otis (*3414*) 1949, and to the extensive literature on pressure-breathing (p. 294).

Paton and Sand (*3736*) 1947 undertook to determine the optimum position for breathing bags or valves in self-contained apparatus and the permissible limits of pressure differences for respiratory

function. They designated the bag pressure which comfortably balanced intrapulmonary pressure as the "eupneic pressure" and expressed this in terms of the position of the bag or demand valve with reference to body landmarks. Eupneic pressure in the standing position at rest was provided when the bag or valve was 5 to 10 cm. below the external auditory meatus, increasing to 10 to 15 cm. with hypernea from any cause. In all other positions, eupneic pressure was attained by positioning the bag or valve at the suprasternal notch. Variations as great as minus 15 or plus 20 cm. had no significant effect on minute volume, tidal air, or shape of the respiratory cycle in the steady state although subjects could readily detect departures from eupneic pressure. The authors also report that vital capacity was reduced by vertical immersion, further reduced by negative intrapulmonary pressure, and partially restored by positive pressure. Reserve air (expiratory reserve volume) was diminished during vertical immersion at eupneic pressure with a corresponding increase in complemental air (inspiratory capacity). Residual air (residual volume) was slightly diminished. In the horizontal position, these volumes were essentially the same as in air.

Karpovich (*3730*) 1939, states that tidal volume of respiration in swimming may vary from less than 0.5 liter to almost 3 liters. He found that the extra work of breathing in water amounted to 2.77 to 5.97 calories per square meter of body surface for each liter of air. This work had an efficiency of 6 to 22.6 percent. The importance of teaching correct breathing in swimming was emphasized by the observations that respiratory movements interfere with propulsion and that improper breathing is apparently capable of disturbing blood pressure to the point of causing headaches and epistaxis in beginners. The study included experiments in breathing while submerged at various depths which indicated that submersion to a depth of 4.25 feet may preclude any possibility of breathing through an open tube to the surface. In a study of the energy requirements of swimming, Karpovich and Millman (*3732*) 1944 discovered that swimming in excess of 2 feet per second (about 1.2 knots) elevated metabolism to more than 10 times the basal rate, while speeds beyond 5 feet per second (about 3 knots) might cause a 100-fold increase. They also reported that untrained swimmers expend 2 to 5 times as much energy as skilled swimmers. The study permitted ranking the various strokes in order of increasing energy costs: crawl, back, breast, and side. The greater fatiguing effect of the butterfly stroke as compared to conventional breast stroke was tentatively explained by greater local fatigue of shoulder-girdle muscles. (Swimming with "fins," using the legs only, which is the style generally used in operational swimming, was not investigated.)

Karpovich and Le Maistre (*3731*) 1940, investigated a method of predicting swimming performance based on a man's maximum oxygen intake, maximum oxygen debt, and oxygen requirements for various speeds. With this information, obtained in test swims of 180 feet or less, it was possible to predict breast-stroke swimming times for distances up to 1,320 feet. They conclude that an improvement in swimming can be obtained only through improved efficiency of the stroke and increased capacity for oxygen intake and debt. The work was confined to one subject. The effect of prior oxygen inhalation on swimming performance was also studied by Karpovich (*3729*) 1934. He states that an increase of speed in the hundred yard dash resulted from oxygen inhalation immediately prior to swimming but not from inhalation 4 to 5 minutes before. The effect apparently lasted about 1 minute, provided the subject remained quiet. Oxygen inhalation after a 100-yard dash appeared to relieve respiratory and circulatory embarrassment but did not influence performance on a second swim 20 minutes later.

An early study of respiration in swimming is that of Aycock, Graaff, and Tuttle (*3724*) 1932, who describe a method of recording respiratory rhythms of swimmers. They found that as stroke rate is increased, both respiratory and expiratory phases are shortened but that the latter shows the greatest change. Saviano and Boeri (*3737*) 1946 compared respiratory and circulatory data in two expert and two less skilled Italian "frogmen." They found that, at rest, the less skilled men had lower blood-oxygen capacity and more variable alveolar carbon dioxide tensions. At work, their oxygen consumption-ventilation ratio was lower (i. e., they tended to increase their ventilation out of proportion to the increase in oxygen consumption) and their circulatory rates were slower. All 4 subjects breathed 100 percent oxygen while working. All experienced syncope, headache, and dyspnea under various circumstances.

Arnold (*3723*) 1937 reports that swimming increases oxygen consumption more than any other sport and that the largest lung capacities are found in trained swimmers. Swimming seriously depletes the alkaline reserve of the blood, according to Hewitt and Calloway (*3727*) 1936. The influence of cold-water swimming on pulse and blood pressure was studied by Miyama (*3734*) 1930–31, who states that pulse rate, systolic pressure, and pulse pressure return gradually to normal after such exertion but that diastolic pressure returns at a

much slower rate. Protein, erythrocytes, and leukocytes, previously absent, were found in the urinary sediment of many subjects after swimming. Vladysik and Turkeltaub (*3739*) 1936 attribute electrocardiographic changes in swimming to a shift of the blood volume, the rate of return to normal being influenced by the duration and intensity of exertion as well as individual differences in cardiovascular apparatus.

Lanoue (*3733*) 1950 studied swimming cramps and concluded they are not very likely to occur in usual indoor swimming and are of little consequence to trained swimmers unless speed or power is required. Most cramps occur in the calf of the leg and can be remedied (or prevented in the incipient stage) by stretching the affected muscle. Lanoue states that stomach cramps are probably much overrated as a factor in drowning. He also concludes that the amount of fat, minor variations of water temperature, and swimming ability have little influence on the occurrence of cramps and that swimming directly after meals has no harmful effects on college indoor swimmers except when speed is required. Muido (*3735*) 1946 found that improved swimming speed resulted from increasing the rectal temperature by passive (hot bath) or active (exercise) warming prior to swimming. Active warming was the most effective. An increase of 0.6° C. in rectal temperature from stationary bicycling improved the time by 1.4 to 2.6 percent. Lowering the temperature by 1° C. decreased efficiency by 3.6 to 6.3 percent.

For further studies related to swimming, reference should be made to papers by Dummer (*3726*) 1940; Zosiaka (*3740*) 1943; Jaedicke (*3728*) 1937; and Akashi (*3711* and *3712*) 1951.

3723. Arnold A. Zur physiologie des Schwimmens. *Gesundh. u. Erzieh.*, 1937, *50:* 39–44. [D]

3724. Aycock, T. M., L. H. Graaff and W. W. Tuttle. An analysis of the respiratory habits of trained swimmers. *Res. Quart. Amer. phys. Educ. Ass.*, 1932, *3:* 199–217. [P]

3725. Dannehi, ( ). Ohr und Schwimmdienst. *Dtsch. Militararzt.*, 1912, *41:* 418–422. [D]

3726. Dummer, G. Die gesundheitliche Bedeutung des Schwimmsportes. *Med. Welt*, 1940, *14:* 168–170. [D]

3726–a. Fenn, W. O. Mechanics of respiration. *Amer. J. Med.*, 1951, *10:* 77–91.

3727. Hewitt, J. E. and E. C. Callaway. Alkali reserve of the blood in relation to swimming performance. *Res. Quart. Amer. phys. Educ. Ass.*, 1936, *7:* 83–93. [P]

3728. Jaedicke, H. G. Aus dem arztlichen Schrifttum zur physiologie des Schwimmens. Gesundh. u. Erzieh., 1937, *50:* 52–53. [D]

3729. Karpovich, P. V. The effect of oxygen inhalation on swimming performance. *Res. Quart. Amer. phys. Educ. Ass.*, 1934, *5:* 24–30. [P]

3730. Karpovich, P. V. Respiration in swimming and diving. *Res. Quart. Amer. phys. Educ. Ass.*, 1939, *10:* 3–14.

3731. Karpovich, P. V. and H. Le Maistre. Prediction of time in swimming breast stroke based on oxygen consumption. *Res. Quart. Amer. phys. Educ. Ass.*, 1940, *11:* 40–44. [P]

3732. Karpovich, P. V. and N. Millman. Energy expenditure in swimming. *Amer. J. Physiol.*, 1944, *142:* 140–144. [P]

3733. Lanoue, F. Some facts on swimming cramps. *Res. Quart. Amer. phys. Educ. Ass.*, 1950, *21:* 153–157. [P]

3734. Miyama, A. [Investigation into the influence of bodily exercise on the function of the circulatory system. V. The influence of cold-water swimming upon the pulse rate and blood pressure.] *Acta Sch. med. Univ. Kioto,* 1930/31, *13:* 51–55 (English pagination). [P]

3735. Muido, L. The influence of body temperature on performances in swimming. *Acta physiol. scand.*, 1946, *12:* 102–109. [P]

3736. Paton, W. D. M. and A. Sand. The optimum intrapulmonary pressure in underwater respiration. *J. Physiol.*, 1947, *106:* 119–138.

3737. Saviano, M. and E. Boeri. Osservazioni su "sommozzatori". *Arch. Sci. biol. Napoli,* 1946, *31:* 29–38.

3738. Stafford, J. Protect your sinuses. Precautions necessary when swimming because humans lack workable muscle for closing nostrils in water. *Sci. News Lett., Wash.*, 1941, *40:* 90–91.

3739. Vladysik, M. M. and M. Turkeltaub. O vliianii morskikh kupanii i dalnikh zaplyvov na serdechno-sosudistuiu sistemu. [The effect of ocean bathing and distance swimming on the cardiovascular system.] *Terap. Arkh.*, 1936, *14:* 609–623. [P]

3740. Yosioka, Z. [The influence of swimming on the functions of the body—the changes in gases (O_2 and CO_2) with fresh water swimming and different types of swimming.] *Keio Igaku*, 1943, *23:* 1143–1161. (English text pagination.)

III. DISEASES PREVALENT IN SWIMMERS

The most common infections found to occur in personnel in swim-diving while operating in warm, moist climates are those attributed to the fungi. The ears, feet, hands, and groins are the sites most commonly affected. Dermatomycoses, or fungus affections of the skin, include all the pathologic alterations of the skin and/or its appendages which are produced by fungi or their products.

A discussion of fungus infections found in swimmers operating in tropical waters is given in a paper by Waite (*3721*) 1951. Otomycosis, a subacute or chronic mycotic infection of the ear, is characterized by an exudate. The common complaint is pruritis and pain, especially at night. Hearing is frequently impaired, and in the subacute phase the external auditory meatus may be swollen shut, red, and weeping and the entire ear may be exquisitely tender to palpation. A superimposed secondary bacterial infection is not uncommon. The author

recommends treatment of a soothing nature for the acute phase: compresses applied to reduce edema and irrigation of the external canal with a solution of hydrogen peroxide and sodium bicarbonate. Wicks saturated with Burow's solution should be placed in the canal. When the infection has subsided the affected parts should be painted with 1 percent gentian violet.

While on a training cruise with an underwater demolition team in a semitropical climate Waite instituted a program to prevent fungus infections. After every swim the ears were swabbed dry and a fungicidal powder (undecylenic acid and zinc undecylenate) was blown into the external auditory meatus with an atomizer. In a 6-week period, during which the personnel involved were in the water almost every day, there were no cases of fungus infection of the ears as compared with the high incidence observed on previous trips to the same area. The following important factors predisposing to fungus infection have been listed by Pillsbury, Sulzberger, and Livingood (*3760*) 1942: (1) excessive sweating; (2) circulatory instability or vascular disease of the extremities; (3) encasement of the feet in heavy shoes; (4) prolonged wearing of foot gear; and (5) extended immersion. Further studies of fungus infections and therapy have been reported by Conant, Martin, Smith, Baker, and Callaway (*3743*) 1944; Dowding and Levy (*3744*) 1939; Downing and Conant (*3745*) 1945; Duggan (*3746*) 1944; Frazier and Leeper (*3747*) 1950; Glauser (*3749*) 1944; Gohar and Manson-Bahr (*3750, 3751*) 1948; Haley (*3752, 3753, 3754,* and *3755*) 1950; James (*3756*) 1943; Lewis (*3758*) 1951; Peck (*3759*) 1943; Shattuck (*3762*) 1951; Smith (*3763*) 1949; Sneddon (*3764*) 1942; Sutton and Sutton (*3765*) 1951; Swartz (*3766*) 1949; Whalen (*3767*) 1938; Wiltshire (*3768*) 1944; and Wolf (*3769*) 1945.

In addition to fungus infections, acute bacterial infections of the external ear contribute to the reduction of the total number of man-hours in operational swim-diving. For a description of acute bacterial infection of the external ear, a paper by Mitchell (*3756a*) 1937 may be consulted. At times the condition is clinically indistinguishable from the early phase of otomycosis. A small furuncle may be found if the infection is seen early but in the later stages the edema and tenderness make thorough examination of the ear impossible. The ear drum is normal in appearance and if it can be visualized no discharge can be seen. Treatment consists of hot compresses to reduce edema and either penicillin or sulfadiazine for the infection.

An unusual condition found in swimmers exposed to cold water is reported by Adams (*3741* and *3742*) 1951. Lowering the external auditory canal temperature to approximately 65° F. by cold water is stated to be a major contributing factor in the development of exostoses and hyperostoses of the bony meatus.

For further articles concerned with clinical problems encountered in swimming the reader is advised to consult reports by the following authors: Davies (*3748*) 1938; Mood, Clarke, and Gelperin (*3757*) 1951; and Rochaix (*3761*) 1936.

3741. Adams, W. S. The aetiology of swimmer's exostoses of the external auditory canals and of associated changes in hearing. Part. I. *J. Laryng.*, 1951, *65:* 133–153. [D] [CH]

3742. Adams, W. S. The aetiology of swimmer's exostoses of the external auditory canals and of associated changes in hearing. Part II. *J. Laryng.*, 1951, *65:* 232–250. [CH]

3743. Conant, Norman F., Donald Stover Martin, David Tillerson Smith, Roger Denio Baker, and Jasper Lamar Callaway. *Manual of clinical mycology.* Philadelphia, W. B. Saunders Company, 1944, 348 pp.

3744. Dowding, E. S. and M. R. Levy. A mould from the ear. *Canad. med. Ass. J.*, 1939, *41:* 336–339.

3745. Downing, J. G. and N. F. Conant. Mycotic infections. *New Engl. J. Med.*, 1945, *233:* 153–161.

3746. Duggan, T. L. Investigation of the fungistatic activity of reagents that might be suitable for use in the treatment of epidermophytosis. U. S. Navy. NMRI. *Project X–469, Rept. no. 1,* 5 October 1944, 4 pp.

3747. Frazier, C. N. and R. W. Leeper. The treatment of common skin diseases. *Med. Clin. N. Amer.*, 1950, *34:* 1473–1486.

3748. Daviess, G. B. Sinusitis and ear infections as related to swimming and diving. *J. Hlth. phys. Educ.*, 1938, *9:* 308.

3749. Glauser, F. Management of fungus infection of the feet. *Nav. med. Bull., Wash.*, 1944, *43:* 525–526.

3750. Gohar, N. and P. Manson-Bahr. The mycoses. pp. 14–16 in: *Mycoses and practical mycology.* Baltimore, The Williams & Wilkins Company, 1948, 234 pp.

3751. Gohar, N. and P. Manson-Bahr. Fungicides: fungistatics: prescriptions: media: poisonous fungi. Pp. 209–221 in: *Mycoses and practical mycology.* Baltimore, The Williams & Wilkins Company, 1948, 234 pp.

3752. Haley, L. D. Etiology of otomycosis. I. Mycologic flora of the ear. *Arch. Otolaryng.*, Chicago, 1950, *52:* 202–207.

3753. Haley, L. D. Etiology of otomycosis. II. Bacterial flora of the ear. *Arch. Otolaryng.*, Chicago, 1950, *52:* 208–213.

3754. Haley, L. D. Etiology of otomycosis. III. Observations on attempts to induce otomycosis in rabbits. *Arch. Otolaryng.*, Chicago, 1950, *52:* 214–219.

3755. Haley, L. D. Etiology of otomycosis. IV. Clinical observations. *Arch. Otolaryng.*, Chicago, 1950, *52:* 220–224.

3756. James, A. P. R. The fungi go to war. *Nav. med. Bull., Wash.*, 1943, *41:* 1065–1067.

3756–a. Mitchell, J. H. Streptococci dermatoses of the ears. *J. Amer. med. Ass.*, 1930, *108:* 361–366.

3757. Mood, E. W., C. C. Clarke, and A. Gelperin. The effect of available residual chlorine and hydrogen-ion concentration upon the eyes of swimmers. *Amer. J. Hyg.*, 1951, *54:* 145–159. [P]

3758. Lewis, G. M. Superficial fungous infections. pp. 665–671 in: The specialties in general practice. Edited by Russell L. Cecil. Philadelphia, W. B. Saunders Company, 1951, 818 pp.

3759. Peck, S. M. A practical plan for the treatment of superficial fungus infections. *Publ. Hlth. Rep., Wash.*, 1943, *58:* 337–345.

3760. Pillsbury, Donald M., Marion B. Sulzberger, and Clarence S. Livingood. Fungous infections. pp. 201–219 in: *Manual of dermatology.* Philadelphia. W. B. Saunders Company, 1942, 421 pp.

3761. Rochaix, A. Natation et dangers d'infection. *C. R. Congr. int. Méd. éduc. phys.* (*1934*) *1936,* pp. 331–336. [D]

3762. Shattuck, George Cheever. Dermatomycoses. pp. 623–629 in: *Diseases of the tropics.* New York, Appleton-Century-Crofts, Inc., 1951, 803 pp.

3763. Smith, D. T. Fungous infections in the United States. *J. Amer. med. Assoc.*, 1949, *141:* 1223–1225.

3764. Sneddon, I. B. Epidermophyton infections of the skin. *J. R. nav. med. Serv.*, 1942, *28:* 154–160.

3765. Sutton, R. L. and R. L. Sutton, Jr. The mycoses. pp. 115–170 in: *Practice of medicine.* Volume 4. Edited by Frederick Tice. Hagerstown, W. F. Prior Company, Inc., 1951, 733 pp.

3766. Swartz, Jacob Hyams. *Elements of medical mycology.* Second edition. New York, Grune & Stratton, 1949, 240 pp.

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3768. Wiltshire, S. P., C. Wilcocks, and J. T. Duncan. *An annotated bibliography of medical mycology 1943.* Kew, Surrey, The Imperial Mycological Institute, 1944, 32 pp. [B]

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IV. HAZARDS FROM DANGEROUS FISH AND OTHER MARINE ORGANISMS

The underwater swimmer working in tropical waters has as much to fear from invertebrate animals such as barnacles, coral, jellyfish, and sea urchins, as from vertebrates such as barracudas, sharks, and seals. The Moray eels will bite severely if molested and sting rays will inflict a wound if stepped on. According to Levin and Behrman (*3780*) 1941, abrasions by coral are notoriously slow to heal and it has been supposed that a toxic material on the coral is responsible. The affected skin shows intense serous exudation and a sloughing ulcer may appear within 24 hours. Immediate cleansing of all abrasions with soap and water, followed by application of sulfanilamide powder and dry dressings will aid prompt healing. Lambertsen (*3718*) 1947 recommends that when cases of retarded healing occur, treatment should consist in restriction from water work, cleansing of the ulcer with a three-percent solution of hydrogen peroxide, and a dry dressing.

A very large jellyfish or a concentration of jellyfish can incapacitate the operator and cause failure of the mission. On the tentacles of the jellyfish are thousands of specialized cells called nematocysts which are concerned with food getting. When the small sensitive elements of the nematocyst are touched a microscopic barb is projected to pierce the prey. The injected toxin is capable of paralyzing small fish and other life. A report of two jellyfish sting cases in 1943 by Stuart and Slagle (*3786*) describes pain of a burning character at the site of contact, with redness followed by an urticaria-like wheal about 10 minutes later. A person stung by jellyfish experiences immediate, severe pain usually accompanied by nausea and weakness and possibly shock. Moderate dilatation of the pupils may be accompanied by congestion of the respiratory mucous membrane and spasm of the respiratory muscles. The authors recommended intravenous use of 10 cu. cm. of 10 percent calcium gluconate. Since this is usually not practical in the field, no treatment beyond local cold compresses, analgesics and rest may be available to swim-divers stung by jellyfish.

Frachtman and McCollum (*3776*) 1945 reported the case of a sailor who was stung by a Portuguese man-of-war across the arms and thighs. Severe muscular spasms ensued, followed by the threat of respiratory failure. Administration of calcium salts intravenously failed to relieve the muscular spasms but barbiturates appeared to be of value in controlling them. For additional information on jellyfish poisoning, reports by Light (*3781*) 1914, Old (*3782*) 1908, and Wade (*3788*) 1928 may be consulted.

Sea urchins (*Strongylocentrotus drobachiensis*) are found in large numbers along coral reefs in tropical waters. According to Waite (*3721*) 1951 it is not uncommon for a swimmer to come away from an encounter with a sea urchin with 30 or more spines in his skin. These spines, which vary from about 2 to 15 cm. in length, have hundreds of microscopic barbs, making extraction difficult. The unfortunate diver who steps or sits on one of these animals suffers a severe, stinging pain as the spines penetrate deep into his tissues and break off. Broken spines buried deeply in the skin may be left alone for they will be absorbed. After the removal of as many spines as possible, the area should be cleansed with an antiseptic solution and cushioned with a large dressing. Penicillin and sulfadiazine should be administered prophylactically because the spines carry bacteria deep into the tissues. Waite recom-

mends wearing canvas shoes to protect the feet from both sea urchins and coral.

The shark problem resembles somewhat the dog problem ashore and it is recommended that the swimmer in shark-inhabited areas keep moving and not become panicky. Actual instances of attacks on man by sharks are rare. Lambertsen (*3718*) 1947 states that the two species apparently guilty of attack on man are the tiger and gray nurse sharks. Experiences of operational swimmers tend to support the impression that sharks exhibit primarily a nonaggressive behavior towards man under the water's surface. Lambertsen reported no cases of shark attack on men operating with him during 10,000 man-hours of swim-diving in the Caribbean Sea, Indian Ocean, and Bay of Bengal. Although large sharks of unidentified species approached within a few feet of divers on many occasions, in each instance the approach was leisurely and in no way resembled an attack. Because it is believed that the shark is excited by the presence of blood in the water, any diver suffering a laceration was required to leave the water. A report by Springer (*3784*) 1943 describes with pictures and geographic location the habits and size of the various generic members of the shark family.

Shark repellents, aside from their actual protective qualities, give a boost to the morale of personnel in or near shark-infested waters. Springer, McBride, Todd, and Schmidt (*3785*) in 1943 reported on the effectiveness of copper acetate diffusing at a rate of 0.1 lb. per hour or more, under the field conditions experienced at that time, acting as a shark repellent. In tests performed by the U. S. Navy (*3787*) 1943, ethanol extract and maleic anhydride were found to be ineffective as shark repellents. Decomposition of shark meat yielded ammonium acetate suggesting the use of copper acetate. The latter compound proved effective as a deterrent when the diffusion rates exceeded 0.1 lb. per hour. The shark repellent (specification no. Mil.–S–2785) attached to the inflatable life jackets of naval aviators includes copper acetate, a black dye, and a wax binder. Further references on the hazards from marine life by the following authors may be consulted: Amaral (*3770*) 1951; Bayley (*3771*) 1940; Burden (*3772*) 1945; Clench and Kondo (*3773*) 1943; Evans (*3774*) 1921; Gudger (*3775*) 1930; Halstead and Modglin (*3777*) 1950; Halstead (*3778*) 1951; Jarcho and Van Burkalow (*3779*) 1951 and Shattuck (*3783*) 1951.

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3783. Shattuck, George Cheever. Various noxious animals. pp. 755–760 in: *Diseases of the tropics.* New York, Appleton-Century-Crofts, Inc., 1951, 803 pp.

3784. Springer, S. Sharks and their behavior. U. S. Navy. Office of coordinator of research and development. Emergency rescue equipment section, Washington, D. C., 29 September 1943, 10 pp. [R]

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V. UNDERWATER BREATHING APPARATUS AND RELATED GEAR

For many underwater operations, the advantages of apparatus independent of surface connections are obvious. Work requiring mobility, stealth, or freedom from heavy surface equipment can be carried out expeditiously with suitable self-contained underwater breathing apparatus. For a valuable review of such equipment, the reader is referred to

sections of a lengthy monograph by Davis (*3713, 3797*) published in 1951.

Development of self-contained underwater breathing apparatus has followed three major lines: (1) the closed-circuit apparatus; (2) the open-circuit apparatus; and (3) the semi-closed circuit apparatus. These resulting types of equipment have characteristics which are distinct and which are advantageous in some types of work and undesirable in others. The first type in general use was the closed-circuit (oxygen rebreathing) equipment, the elements of which are a cylinder of oxygen, a breathing bag, and a canister containing a carbon dioxide absorbent. Such apparatus has the advantages of virtually complete utilization of the gas which is carried and the resulting absence of bubbles. It is thus well adapted to work where the presence of the user must not be detected from the surface. The main disadvantage lies in the possibility of oxygen poisoning, which strictly limits the depth at which it can be safely used.

Blockwick (*3790* and *3792*) 1950 reports comparative evaluations of 3 closed-circuit units; Lambertsen, Mine Safety Appliance Co., and Browne. The studies included swimming runs with determination of oxygen and carbon dioxide levels and overall endurance. Breathing resistance, dead air space, and the visual angles of mask eyepieces were measured, and general ease of use and repair were evaluated. Improvements in the Lambertsen unit were discussed in a U. S. Army report (*3803*) in 1951. Modifications included increased operating duration through larger oxygen supply and increased carbon dioxide absorption capacity, incorporation of a demand valve for automatic oxygen supply and buoyancy control, and improved vision through the use of smaller eyepieces mounted closer to the eyes. Report 3807 includes historical material on self-contained breathing equipment and describes the Pirelli closed-circuit apparatus. This employs a valve system intended to supply oxygen at a constant rate. Waite (*3806*) 1951 reports an American evaluation of a British closed-circuit unit known as the Varbell.

Perhaps the simplest form of self-contained underwater breathing apparatus is that which consists of cylinders containing compressed air with a demand valve which releases the amount of air required for each inspiration. Since the exhaled breath is simply expelled into the water, the term "open-circuit" is generally applied to this type of equipment. The volume of gas which must be carried for a dive of given duration is obviously much larger than for closed-circuit equipment. The duration of the supply is further diminished at greater depths where the respiratory volume remains relatively unchanged while the elevated ambient pressure increases the actual mass of gas removed from the cylinders by each inspiration. Open-circuit apparatus can be used at much greater depths than oxygen-rebreathing systems, depth limits being imposed primarily by duration of the air supply and by the danger of decompression sickness. Talliez, Dumas, Cousteau, Alinat, and Devilla (*3802*) 1949, include in their monograph on diving a discussion of the problems and principles of design of open-circuit apparatus.

In his evaluation of open-circuit apparatus, Blockwick (*3794*) 1950, emphasizes the simplicity of this equipment but calls attention to the increased breathing resistance which demand valves may offer under conditions of hard work and increased depth. He also stresses the desirability of limiting the use of such units to those depths and times which do not require stage decompression. For further information on open-circuit compressed air equipment, reference may be made to Fulton and Blockwick (*3798*) 1951, Bussoz (*3796*), and reports 3800 and 3801.

The third major type of self-contained underwater breathing apparatus involves a "semi-closed" circuit in which the gas supply is conserved by rebreathing but in which a controlled rate of inflow and spillage permits reasonably safe use of breathing media other than pure oxygen. Reports by Waite (*3805*) 1951, and Fulton, Welham, and Blockwick (*3799*) 1951, discuss the performance of such equipment and point out its advantages over the simpler open- and closed-circuit types. The percentage of nitrogen in the respired gas, and thus also the danger of decompression sickness, can be reduced by using a gas mixture containing a higher percentage of oxygen than that found in air. Provided that the increase in oxygen content is not sufficient to introduce the danger of oxygen poisoning and that consumption of oxygen does not exceed the amount supplied, use of this apparatus permits significant extension of the depth-time limits. In addition, the reduction of bubble formation renders detection more difficult than in the use of open-circuit gear. Reference may also be made to Blockwick (*3789* and *3793*) 1950, and report 3804 for further information on subjects relating to self-contained underwater breathing apparatus.

In many locations, the effect of exposure to cold water limits the activities of swim-divers much more severely than do problems of breathing apparatus. Development of protective suits is thus a vital task which demands extensive study. Problems of buoyancy-control introduced by the use of insulating

suits to conserve body heat can be discerned in a study by Blockwick (*3791*) 1950, in which a lightweight diving dress and an underwater swim suit were investigated from this standpoint with various amounts of clothing beneath. The obvious advantages of a positive method of supplying heat led to an investigation of electrically heated clothing by Blockwick (*3795*) 1951. It was concluded that 150 to 250 watts are required to keep hands and feet warm in water colder than 45° F. and that it is not feasible for a swimmer to carry batteries which will meet these power requirements. The study also indicated that two suits of heavy diving underwear would suffice without additional heat in water at 55° F., but that immersion at 45° F. would require the same amount of underwear in addition to heated gloves and boots.

3789. Blockwick, T. N. Determination of the potentialities of the mine safety appliance self-contained swimming outfit for descents to 400 ft. using helium-oxygen breathing mixtures. U. S. Navy. Naval gun factory. EDU. *S94–(3)–(1)–(694D) of 4 November 1949, Rept. no. 10–50,* 4 December 1950.

3790. Blockwick, T. N. Determination of CO_2 and O_2 at various stages of the dives using 3 different types of self-contained breathing apparatus under identical conditions and the appraisal of them from a standpoint of comfort, breathing resistance, duration, visibility and other factors pertinent to their practical use. U. S. Navy. Naval gun factory. EDU. *Project NS 186–012, Rept. no. 1–50,* 21 February 1950, 8 pp.

3791. Blockwick, T. N. The determination of the basic condition of lightness that can be attained by the present lightweight diving outfit and the underwater swim suit and the evaluation of their operating characteristics. U. S. Navy. Naval gun factory. EDU. *Project NS 186–052, Rept. no. 2–50,* 21 March 1950, 9 pp.

3792. Blockwick, T. N. Determination of CO_2 and O_2 at various stages of the dives using three different types of self-contained breathing apparatus under identical conditions and the appraisal of them from a standpoint of comfort, breathing resistance, duration, visibility and other factors pertinent to their practical use. U. S. Navy. Naval gun factory. EDU. *Project NS 186–012, Rept. no. 4–50,* 12 June 1950, 10 pp.

3793. Blockwick, T. N. Determination of the potentialities of the Bendix, MSA and Cousteau-Gagnon demand breathing appliances for descents to 400 feet and the measurement of the amounts of gas required for the various depths. U. S. Navy. Naval gun factory. EDU. *S94–(3)–(1)–(694D) of 4 November 1949, Rept. no. 5–50,* 2 August 1950, 9 pp.

3794. Blockwick, T. N. Evaluation of the performance of the aqua lung self-contained swimming outfit as furnished and also when it is modified by the substitution of the mouthpiece for a face mask. U. S. Navy. Naval gun factory. EDU. *Project NS–186–012, Test no. 17, Rept. no. 6–50,* 12 September 1950, 5 pp.

3795. Blockwick, T. N. Test of electrically heated clothing. U. S. Navy. Naval gun factory. EDU. *Project NS 186–012, Test no. 12, Rept. no. 3–51,* 13 February 1951, 15 pp.

3796. Bussoz, R. *Self-contained diving.* U. S. Divers Co., Los Angeles, Calif. (no date), 23 pp.

3797. Davis, Robert H. Self-contained and armoured diving apparatus. pp. 204–213 in: *Deep diving and submarine operations. A manual for deep sea divers and compressed air workers.* London, The Saint Catherine Press Ltd., Fifth edition, 1951, 670 pp. [D]

3798. Fulton, H. T. and T. N. Blockwick. Test of the Scott model 8300 self-contained underwater breathing apparatus. U. S. Navy. Naval gun factory. EDU. *Project NS 186–012, Test no. 23, Rept. no. 9–51,* 22 June 1951, 6 pp.

3799. Fulton, H. T., W. Welham and T. N. Blockwick. Preliminary report of nitrogen-oxygen self-contained underwater breathing equipment. U. S. Navy. Naval gun factory. EDU. *Project NS 186–201, Sub task no. 5, Rept. no. 8–51,* 11 June 1951, 13 pp.

3800. Scott Aviation Corporation. Descriptive specifications of the Scott model 8300 self-contained shallow water diving equipment. Lancaster, New York. (no date), 10 pp.

3801. Siebe, Gorman, and Company, Ltd. "Essjee" self-contained compressed air diving apparatus (single cylinder type). *Descriptive information circular.* Siebe, Gorman and Company, Ltd., London, 1 p.

3802. Tailliez, P., F. Dumas, J. Y. Cousteau, J. Alinat, and F. Devilla. Principe des scaphandres. Scaphandres a casque. pp. 23–36 in: *La plongee en scaphandre.* Paris, Elzevir, 1949, 119 pp.

3803. U. S. Army. Engineer research and development laboratory. Fort Belvoir, Va. Water Supply Equipment branch. Improvement of Lambertsen type diving unit. *Project 8–80–11–002, Final rept.,* 1 October 1951, 44 pp.

3804. U. S. Navy. BuShips. Use of shallow water diving mask. *NavShips No. 394 0007,* 1943, 18 pp.

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3806. Waite, C. L. Evaluation of the British Varbell self-contained swimming suit. U. S. Navy. Naval gun factory. EDU. *Project NS 186–012, Rept. no. 4–51,* 2 March 1951, 4 pp.

3807. Anon. Pirelli underwater oxygen self-contained breathing apparatus. Model L. S. 901. Pirelli, Inc. New York, N. Y., 19 pp.

Key to Abbreviations of Journals and Handbooks Cited

Abbreviations not included in *A World List of Scientific Periodicals Published in the Years 1900–50, 3d Ed.*, London, 1952 are marked with an asterisk

Abstr. Diss. Stanf. Univ. Abstracts of Dissertations for the Degree of Doctor of Philosophy. Stanford University, Palo Alto.

Abstr. World Med. Abstracts of World Medicine. London.

Acta brev. neerl. Physiol. Acta brevia Neerlandica de Physiologia, Pharmacologia, Microbiologia, e. a. Amsterdam.

Acta cardiol., Brux. Acta Cardiologica. Bruxelles.

Acta med. scand. Acta medica Scandinavica. Stockholm.

Acta neurol. belg. Acta neurologica et psychiatrica Belgia. Bruxelles.

Acta opthal., Kbh. Acta opthalmologica. Kjøbenhavn.

Acta oto-laryng., Stockh. Acta otolaryngologica. Stockholm.

Acta oto-rhino-laryng. belg. Acta oto-rhino-laryngologica Belgica. Bruxelles.

Acta path. microbiol. scand. Acta pathologica et microbiologica Scandinavica. København.

Acta pharm. toxicol., Kbh. Acta pharmocologica et toxicologica. København.

Acta physiol. pharm néerl. Acta physiologica et pharmacologica Neerlandica. Amsterdam.

Acta physiol. scand. Acta physiologica Scandinavica. Stockholm.

Acta psychiat., Kbh. Acta psychiatrica et neurologica. Kjøbenhavn.

Acta Sch. med. Univ. Kioto. Acta Scholae Medicinalis Universitatis Imperialis in Kioto. Kioto.

Advanc. internal Med. Advances in Internal Medicine. New York.

Advanc. Sci., Lond. Advancement of Science, London.

*Air sea-rescue Bull.** Air sea-rescue Bulletin. Washington D. C.

Air Surg. Bull. Air Surgeon's Bulletin. Dayton, Ohio.

Algérie. med. Algérie médicale. Alger.

Amer. Anthrop. American Anthropologist. Lancaster, Pa.

Amer. Heart J. American Heart Journal. St. Louis.

Amer. ind. Hyg. Ass. Quart. American Industrial Hygiene Association Quarterly.

Amer. J. clin. Path. American Journal of Clinical Pathology. Baltimore.

Amer. J. Hyg. American Journal of Hygiene. Baltimore.

Amer. J. Med. The American Journal of Medicine. New York.

Amer. J. med. Sci. American Journal of the Medical Sciences. Philadelphia.

Amer. J. Nurs. American Journal of Nursing. Philadelphia.

Amer. J. Obstet. Gynec. American Journal of Obstetrics and Gynecology. St. Louis.

Amer. J. Ophthal. American Journal of Ophthalmology. St. Louis.

Amer. J. Optom. The American Journal of Optometry. Minneapolis.

Amer. J. Path. American Journal of Pathology. Boston.

Amer. J. Physiol. American Journal of Physiology. Boston.

Amer. J. Psychol. American Journal of Psychology. Worcester.

Amer. J. publ. Hlth. American Journal of Public Health. New York.

Amer. J. Roentgenol. American Journal of Roentgenology (and Radium Therapy). New York.

Amer. J. trop. Med. American Journal of Tropical Medicine. Baltimore.

Amer. Practit. American Practitioner. Philadelphia.

Amer. Psychol. The American Psychologist. Baltimore.

*Amer. Publ. Hlth. Yearbk, Pt. II.** American Public Health Association Yearbook. New York.

Amer. Rev. Sov. Med. American Review of Soviet Medicine, New York.

An. Fac. Med. Lima. Anales de la facultad de Medicina. Universidad (nacional Mayor de San Marcos) de Lima.

Analyst. The Analyst. London.

Anat. Rec. Anatomical Record. Philadelphia.

Anést. Analg. Anésthesie et analgésie. Paris.

Anesthesiology. Anesthesiology. Lancaster, Pa.

Ann. Hyg. publ., Paris. Annales d'hygiène publique et de médecine légale (industrielle et sociale). Paris.

Ann. intern. Med. Annals of Internal Medicine. Ann Arbor.

Ann. Med. exp. Fenn. Annales medicinae experimentalis et biologiae Fenniae. Helsinki.

Ann. Méd. lég. Annales de médecine légale. Paris.

Ann. Med. nav. colon. Annali di medicina navale e coloniale. Roma.

Ann. N. Y. Acad. Sci. Annals of the New York Academy of Sciences. N. Y.

Ann. Oculist., Paris. Annales d'oculistique. Paris.

Ann. Oto-laryng. Annales d'otolaryngologie. Paris.

Ann. Otol., etc., St. Louis. Annals of Otology, Rhinology and Laryngology. St. Louis.

Ann. trop. Med. Parasit. Annals of Tropical Medicine and Parasitology. Liverpool.

Année psychol. Année psychologique. Paris.

Annu. Rev. med. Annual Review of Medicine. Stanford University, Palo Alto.

Annu. Rev. Physiol. Annual Review of Physiology. Stanford University, Palo Alto.

Arch. Anthrop. crim. Archives d'anthropologie criminelle, de médecine légale et de psychologie normale et pathologique, Lyon.

Arch. belges Med. soc. Archives belges de médecine sociale, hygiène, médecine du travail et médecine légale. Bruxelles.

Arch. Biochem. Archives of Biochemistry. New York.

Arch. Derm. Syph., N. Y. Archives of Dermatology and Syphilology. New York.

Arch. exp. Path. Pharmak. Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie. Leipzig.

Arch. industr. Hyg. Archives of Industrial Hygiene and Occupational Medicine. Baltimore.

Arch. indust. Hyg., Chicago. Archives of Industrial Hygiene. Chicago.

Arch. int. Pharmacodyn. Archives internationales de pharmacodynamie (et de thérapie). Bruxelles-Paris, Gand.

Arch. int. Physiol. Archives internationales de physiologie. Liége et Paris.

Arch. intern. Med. Archives of Internal Medicine. Chicago.

Arch. Mal. prof. Archives des Maladies professionelles; Hygiène et Toxicologie industrielles. Paris.

Arch. Mal. prof. Archives des maladies professionelles de Medecine du travail et de securite sociale. Paris.

Arch. néerl. Physiol. Archives néerlandaises de physiologie de l'homme et des animaux. Amsterdam.

Arch. Neurol. Psychiat., Chicago. Archives of Neurology and Psychiatry. Chicago.

Arch. Ohr.-, Nas.-, u. KehlHeilk. Archiv für Ohren—, (Nasen— und Kehlkopf) heilkunde, Leipzig.

Arch. Ophthal., N. Y. Archives of Ophthalmology. New York.

Arch. Ophtal., Paris. Archives d'ophtalmologie. Paris.

Arch. Otol., N. Y. Archives of Otology. New York.

Arch. Otolaryng., Chicago. Archives of Otolaryngology. Chicago.

Arch. Path., Chicago. Archives of Pathology (and Laboratory Medicine). Chicago.

Arch. phys. Med. Archives of Physical Medicine. Omaha.

Arch. Psychol., N. Y. Archives of Psychology. New York.

Arch. Sci. biol., Napoli. Archivio di scienze biologische. Napoli.

Arch. Sci. med. Archivio per le scienze mediche. Torino.

Arch. Soc. oftal. hisp.-amer. Archivos de la Sociedad oftalmologica hispano-americana. Barcelona.

Arch. Surg., Chicago. Archives of Surgery. Chicago.

Arkh. Pat. Arkhiv Patologii. Moskva.

Army med. Bull. Army Medical Bulletin. Carlisle, Pa.

Beitr. path. Anat. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie. Jena.

Bibl. Laeger. Bibliotek for laeger. Published in Kjøbenhavn.

Biochem. J. Biochemical Journal. Cambridge.

Biol. méd. Biologie medical. Paris.

Blood. Blood. The Journal of Hematology. New York.

Boll. Soc. ital. Biol. sper. Bollettino della Societa italiana di biologia sperimentale. Napoli.

Brain. Brain: a journal of neurology. London.

Brit. dent. J. British Dental Journal. London.

Brit. Guiana med. Annu. British Guiana Medical Annual and Hospital Reports. Demerara.

Brit. J. Derm. British Journal of Dermatology (and Syphilis). London.

Brit. J. industr. Med. British Journal of Indutrial Medicine. London.

Brit. J. Opthal. British Journal of Ophthalmology. London.

Brit. J. phys. Med. British Journal of Physical Medicine and Industrial Hygiene. London.

Brit. J. Psychol. British Journal of Psychology. Cambridge.

Brit. med. Bull. British Medical Bulletin. London.

Brit. med. J. British Medical Journal. London.

Bull. Acad. nat. Méd. Bulletin de l'Académie nationale de médecine. Paris.

Bull. Hyg., Lond. Bulletin of Hygiene. London.

Bull. int. Serv. Santé Arm. Bulletin international des services de santé des armées de terre, de mer et de l'air. Liége.

Bull. Los Angeles neurol. Soc. Bulletin of the Los Angeles Neurological Society. Los Angeles.

Bull. math. Biophys. Bulletin of Mathematical Biophysics. Chicago.

Bull. med. chir. Fac. Md. Bulletin of the Medical and Chirurgical Faculty of Maryland. Baltimore.

Bull. Menninger Clin. Bulletin of the Menninger Clinic. Topeka, Kans.

Bull. New Engl. med. Cent. Bulletin of the New England Medical Centre. Boston, Mass.

Bull. N. Y. Acad. Med. Bulletin of the New York Academy of Medicine. New York.

Bull. pract. Ophthal. Bulletin of Practical Ophthalmology. San Francisco.

Bull. Soc. Franç. Derm. Syph. Bulletin de la Société française de dermatologie et de syphiligraphie. Paris.

Bull. Soc. Franç. Ophtal. Bulletin et mémoires de la Société française d'ophtalmologie. Paris.

Bull. Soc. méd. Hop. Paris. Bulletin et mémoires de la Societe médicale des hôpitaux de Paris.

Byull. eksp. Biol. Med. Byulletin eksperimentalnoy Biologii i Meditsiny. Moskva.

C. R. Acad. Sci., Paris. Compte rendu hebdomadaire des séances de l'-Académie des sciences. Paris.

C. R. Acad. Sci., U. R. S. S. Compte rendu de l'Académie des sciences de l'U. R. S. S. Moskva. Leningrad.

C. R. Congr. int. méd. Educ. Compte rendu; Congres international de Médecine appliquée a l'education physique et aux sports.

C. R. Soc. Biol., Paris. Compte rendu hebdomadaire des séances et mémoires de la Societe de biologie. Paris.

Calif. Med. California Medicine. San Francisco.

Canad. J. Med. Sci. Canadian Journal of Medical Sciences. Ottawa, Canada.

Canad. J. publ. Hlth. Canadian Journal of Public Health. Toronto.

Canad. J. Res. Canadian Journal of Research. Ottawa.

Canad. med. Ass. J. Canadian Medical Association Journal. Toronto.

Cancer Res. Cancer Research. Baltimore.

Čas. Lék. čes. Časopis Lékařů Českých. v Praze.

Chem. Abstr. Chemical Abstracts. Easton, Pa.

Cincinn. J. Med. Cincinnati Journal of Medicine. Cincinnati.

Circulation. Circulation. New York.

Cleveland Clin. Quart. Cleveland Clinical Quarterly. Cleveland.

Clin. Sci. Clinical Science, incorporating Heart. London.

Clin. otorinolaring. Clinica otorinolaringo-iatrica. Roma.

XVI Concil. ophth. 1950 Acta. XVI Concilium Ophthalmologicum 1950 Britannica London Acta. London.
Conn. St. med. J. Connecticut State Medical Journal. New Haven.
Contact. Pensacola. Contact. U. S. Naval Air Station. Pensacola, Fla.
Contr. Boyce Thompson Inst. Contributions from Boyce Thompson Institute for Plant Research. Menasha, Wis.
Curr. Res. Anesth. Current Researches in Anesthesia and Analgesia. Rocky River, Ohio.
Curr. Sci. Current Science. Bangalore.

Dent. Surv. Dental Survey. Minneapolis.
Diagnosi. Napoli. Diagnosi; rivista di medicina pratica. Napoli.
Dis. nerv. Syst. Diseases of the Nervous System. Chicago.
Docum. ophthal. Documenta ophthalmologica. Zurich, Paris.
Dtsch. Militärarzt. Deutsche Militärarzt. Berlin.
Dtsch. militärärztl. Deutsche Militärärztliche Zeitschrift. Berlin.

Endocrinology. Endocrinology. Glendale, Calif.
Engineer, Lond. Engineer. London.
Enzymologia. Enzymologia. Den Haag.
Excerpta med. Excerpta medica. Amsterdam.
Excerpta med. Excerpta medica. Basel, Leipzig.
Experientia. Experientia. Basel.
Exp. Med. Surg. Experimental Medicine and Surgery. Brooklyn Medical Press.

Farmacoter. act. Farmacoterapia actual. Madrid.
Fed. Proc. Federation Proceedings. (American Societies for Experimental Biology). Baltimore.
Fed. Proc. Amer. Soc. Pharm. exp. Ther. Federation Proceedings for the Society for Pharmacology and Experimental Therapeutics, Inc.
Fiziol. Zh. S. S. S. R. Fiziologicheskiy Zhurnal. S. S. S. R. Moskva. Journal of Physiology of the U. S. S. R. Moscow.
Folia cardiol., Milano. Folia cardiologica. Milano.
Folia endocrin. jap. Folia endocrinologica japonica. Kyoto.
Folia med., Napoli. Folia medica. Napoli.
Frankfurt Z. Path. Frankfurter Zeitschrift fur Pathologie. Wiesbaden.
Fukuoka Acta med. Fukuoka Acta medica. Fukuoka.

Gastroenterology. Gastroenterology. Baltimore.
Geneesk. Gids. Geneeskundige Gids.'s Gravenhage.
Geogr. Rev. The Geographical Review. New York.
Gesundh. u. Erzieh. Gesundheit und Erziehung. Leipzig.
Gesundh. u. Wohlf. Gesundheit und Wohlfahrt. Zurich.
Gigiena San., Moskva. Gigiena i sanitariya. Moskva.
Gigiena Truda. Gigiena truda. Moskva.
Gipoksiia. Gipoksiia. Moskva.
Gluckauf. Gluckauf! Berg-u. Huttemann Zeitschrift. Essen.
Guy's Hosp. Gaz. Guy's Hospital Gazette. London.

Heat. Pip. Air Condit. Heating, Piping, and Air Conditioning. New York.
Heat. & Ventilating. Heating and Ventilating. New York.
Helv. med. acta. Helvetica medica acta. Basel.
Helv. physiol. acta. Helvetica physiologica et pharmacologica acta. Basel.
*Hosp. top. & buyer.** Hospital Topics & Buyer. Chicago.
Hospital. Rio de J. Hospital. Rio de Janeiro.
Hum. Biol. Human Biology; a record of research. Baltimore.

Industr. Med. Industrial Medicine. Chicago.
*Igaku & Seibutugaku.** Tokyo.
Illum. Engr., N. Y. Illuminating Engineer. New York.
Indian Physician. Indian Physician. Bombay.
XVIII Intern. physiol. Congr. International Physiological Congress. Copenhagen.
Irish J. med. Sci. Irish Journal of Medical Science. Dublin.

J. acoust. Soc. Amer. Journal of the Acoustical Society of America. Menasha, Wisc.
J. Amer. med. Ass. Journal of the American Medical Association. Chicago.
J. Amer. Wat. Wks. Ass. Journal of the American Water Works Assoc., Baltimore.
J. Anim. Sci. Journal of Animal Science. Menasha, Wisc.
J. appl. Physiol. Journal of Applied Physiology. Washington.
J. appl. Psychol. Journal of applied Psychology. Worcester, Mass.
J. Aviat. Med. Journal of Aviation Medicine. New Orleans.
J. biol. Chem. Journal of Biological Chemistry. Baltimore.
J. cell. comp. Physiol. Journal of Cellular and Comparative Physiology. Philadelphia.
J. Chir., Paris. Journal de chirurgie. Paris.
J. clin. Endocrin. Journal of Clinical Endocrinology. Springfield, Ill.
J. clin. Invest. Journal of Clinical Investigation. Baltimore.
J. clin. Psychol. Journal of Clinical Psychology. Burlington.
J. comp. Psychol. Journal of Comparative Psychology. Baltimore.
J. dent. Res. Journal of Dental Research. Baltimore.
J. Egypt. med. Ass. Journal of the Egyptian Medical Association. Cairo.
J. Endocrin. Journal of Endocrinology. Oxford, Cambridge.
J. exp. Med. Journal of Experimental Medicine. New York.
J. exp. Psychol. Journal of Experimental Psychology. Princeton, N. J.
J. exp. Zool. Journal of Experimental Zoology. Philadelphia.
J. franç. Méd. Chir. thor. Journal français de médecine et chirurgie thoracique. Paris.
J. gen. Physiol. Journal of General Physiology. Baltimore.
J. gen. Psychol. Journal of General Psychology. Worcester, Mass.
J. Geront. Journal of Gerontology. Springfield, Ill.
J. Hlth. phys. Educ. Journal of Health and Physical Education. Springfield, Mass.
J. Hyg., Camb. Journal of Hygiene. Cambridge.
J. Indian med. Ass. Journal of the Indian Medical Association. Calcutta.
J. Ind. med. Ass. Journal of the Indiana State Medical Association. Indianapolis.
J. industr. Hyg. Journal of Industrial Hygiene (and Toxicology). New York, Boston, Baltimore.
J. infect. Dis. Journal of Infectious Diseases. Chicago.
*J. invest. Derm.** Journal of Investigative Dermatology. Baltimore.
J. Lab. clin. Med. Journal of Laboratory and Clinical Medicine. St. Louis.

J. Laryng. Journal of Laryngology (Rhinology) and Otology. London.

J. Méd. Chir. prat. Journal de médecine et de chirurgie pratiques. Paris.

J. Méd. Lyon. Journal de médecine de Lyon.

J. med. Soc. N. J. Journal of the Medical Society of New Jersey. Newark.

J. Ment. Sci. Journal of mental Science. London.

J. Mich. med. Soc. Journal of the Michigan State Medical Society. Detroit.

J. Mie med. Coll. Journal of Mie Medical College.

J. nerv. ment. Dis. Journal of Nervous and Mental Diseases. New York.

J. Neurol. Psychiat. Journal of Neurology (Neurosurgery) and Psychiatry. London.

J. Neuropath. Journal of Neuropathology and Experimental Neurology. Baltimore.

J. Neurophysiol. Journal of Neurophysiology. Springfield, Ill.

J. Nutrit. Journal of Nutrition. Philadelphia, Pa.

J. Okla. med. Ass. Journal of the Oklahoma State Medical Association. Muskogee.

J. opt. Soc. Amer. Journal of the Optical Society of America. Philadelphia.

J. oto-rhinolaryng. Soc., Tokyo. Journal of the Oto-rhino-laryngological Society of Japan. Tokyo.

J. Path. Bact. Journal of Pathology and Bacteriology. London.

J. Pharmacol. Journal of Pharmacology and Experimental Therapeutics. Baltimore.

J. Phil. Is. med. Ass. Journal of the Philippine Islands Medical Association. Manila.

J. Physiol. Journal of Physiology. London; Cambridge.

J. Physiol. Path. gén. Journal de physiologie (et de pathologie générale). Paris.

J. Psychol. Journal of Psychology. Worcester, Mass.

J. R. nav. med. Serv. Journal of the Royal Naval Medical Service. London.

J. Radiol. Electrol. Journal de radiologie et d'electrologie (et Archives d'electricite medicale).

J. Res. nat. Bur. Stand. Journal of Research. National Bureau of Standards. Washington.

J. Sci. Labour. The Journal of Science of Labour. Tokyo.

J. Speech Dis. Journal of Speech (and Hearing) Disorders. Columbus, Ohio.

J. thorac. Surg. Journal of Thoracic Surgery. St. Louis.

*Jap. J. Hyg.** Japanese Journal of Hygiene. Tokyo.

Jap. J. Physiol. Japanese Journal of Physiology. Nagoya.

Jap. med. J. The Japanese Medical Journal. Tokyo.

Johns Hopk. Hosp. Bull. Johns Hopkins Hospital Bulletin. Baltimore.

*Keio Igaku.** Keio Igaku. Tokyo.

Klin, Mbl. Augenheilk. Klinische Monatsblätter für Augenheilkunde. Stuttgart.

*K. Krigsvet. handl. tidsskr.** Kungliga Krigsvetenskaps - akademien Handlingar och tidsskrift. Stockholm.

Lancet. Lancet. London.

Laryngoscope. St. Louis. Laryngoscope. St. Louis.

Laval méd. Laval médical. Québec.

Lek wojsk. Lekarz Wojskowy. Warszawa.

Luftfahrtmedizin. Luftfahrtmedizin. Berlin.

Mag. belorv. Arch. Magyar Belorvosi Archivum es Ideggyogyaszati Szemle. Budapest, Hungary.

Mar. News. Marine News. New York.

Maroc med. Maroc medical. Casablanca.

MD. MD. Chicago.

Mech. Engr. Mechanical Engineer. Manchester.

Méd. aéro. Médicine aéronautique. Paris.

Med. Arts Sci. Medical Arts and Sciences. Washington.

Med. Cirurg. Pharm. Medicina, cirurgia, pharmacia. Rio de Janeiro.

Med. Clin. N. Amer. Medical Clinics of North America. Philadelphia.

Med. d. Lavoro. Medicina del lavoro. Milan.

Med. Departe y Trab. Medicina del deporte y del trabajo. Buenos Aires.

Méd. et Hyg., Anvers. Médecine et hygiène. Anvers.

*Med. Glasn. (Russian).** Medicinski. Glasnik. Belgrade.

Med. J. Aust. Medical Journal of Australia. Sydney.

Med. J. Malaya. Medical Journal of Malaya. Singapore.

Med. J. Rec. Medical Journal and Record. New York.

Med. Klinik. Medizinische Klinik. Wien.

Med. Pr. Medical Press (and Circular). London.

Méd. usine. Le Médecin d'usine. Edition du Médecin d'usine. Paris.

Med. Welt. Medizinische Welt. Berlin.

Med. World. Lond. Medical World. London.

Med. World. Philad. Medical World. Philadelphia.

Medicina. Madr. Medicina. Madrid.

Medicine. Baltimore. Medicine. Baltimore.

Mem. Inst. Osw. Cruz. Memo ias do Instituto Oswaldo Cruz. Rio de Janeiro.

Milit. Rev. Fort Leavenw. Command and General Staff School Military Review. Fort Leavenworth, Kansas.

Milit. Surg. Military Surgeon. Washington.

Mitt. med. Akad. Kioto. Mitteilungen aus der Medizinischen Akademie zu Kioto. Kyoto-Ikadaigaku-Zasshi.

Mschr. Ohrenheilk. Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie. Wien & Berlin.

N. Y. med. J. New York Medical Journal. New York.

N. Y. St. J. Med. New York State Journal of Medicine. New York.

Nat. Inst. Hlth. Bull. National Institute of Health Bulletin. United States Public Health Services. Washington.

Nation's Hlth. Nation's Health. Chicago.

Nature. Lond. Nature. London.

Nature. Paris. Nature. Paris.

*Nav. arm. med. Cps. J.** Naval Army Medical Corps Journal. Washington.

Nav. med. Bull., Wash. Naval Medical Bulletin. Washington.

Nav. med. Res. Inst. Rept. Naval medical Research Institute Reports. Washington.

Ned. milit.-geneesk. Arch. Nederlandsch militairgeneeskundig archief. Utrecht.

Ned. Tijdschr. Geneesk. Nederlandsch tijdschrift voor geneeskunde. Amsterdam.

New Engl. J. Med. New England Journal of Medicine. Boston .

*Nippon rinsyo.** Nippon Rinsyo. Osaka.

Nippon Seiri. Z. Nippon Seirigaky Zassi. Japan.

Nissin Igaku. Nissin Igaku. Tokyo.

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Nord. med. Nordisk medicin. Stockholm.
Nuclear Sci. Abst. Nuclear Science Abstracts. Oak Ridge, Tenn.
Nutrit. Rev. Nutrition Reviews. New York.

Occup. Med. Occupational Medicine. Chicago.
Ophthalmologica. Ophthalmologica. Basel.
Orv. Hetil. Orvosi Hetilap. Honi és külföldi gyógyázat és kórbuvárlat közlönye. Budapest.
Osaka Univ. med. J. Osaka Daigaku Igaku Zassi. Osaka.
Otolaryng. slav. Otolaryngologia slavica. Prag.
*Oto-rhino-laryng., Danub.** Oto-rhino-laryngologica Danubiana. Budapest.

Paris méd. Paris médical. La semaine du clinicien. Paris.
Penn. med. J. Pennsylvania Medical Journal. Pittsburgh.
Personnel J. Personnel Journal. Baltimore.
Pflüg. Arch. ges. Physiol. Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere. Bonn.
Pharm. J. Pharmaceutical Journal and Pharmacist. London.
Pharmacol. Rev. Pharmacological Reviews. Baltimore.
Philipp. J. Sci. (b). Philippine Journal of Science. (b) Medicine. Manila.
Physiol. Rev. Physiological Reviews. Baltimore.
Physiol. Zoöl. Physiological Zoölogy. Chicago.
Physiother., Lond. Physiotherapy. London.
Plast. reconstr. Surg. Plastic and Reconstructive Surgery. Baltimore.
Pol. med. Wkly. Polski Tydgodnik Lekarski. Warszawa.
Policlinico. Policlinico. Roma.
Postgrad. Med. Postgraduate Medicine. Milwaukee.
Pr. méd. Presse médicale. Paris.
Pract. oto-rhino-laryng. Practica oto-rhino-laryngologica. Basel.
Practitioner. Practitioner. London.
Prakt. Lék., Praha. Praktický Lékař. Praha.
Prensa med. argent. Prensa medica argentina. Buenos Aires.
Probl. fiziol. Akust. Problemy Fiziologicheskoi Akustiki. Moskva.
Proc. Amer. phil. Soc. Proceedings of the American Philosophical Society. Philadelphia.
Proc. cent. Soc. clin. Res. Proceedings of the Central Society for Clinical Research. Chicago.
Proc. Mayo Clin. Proceedings of the Staff Meetings of the Mayo Clinic. Rochester, Minn.
Proc. nat. Acad. Sci., Wash. Proceedings of the National Academy of Sciences. Washington.
Proc. ninth intern. congr. industr. med. 1948. Proceedings of the ninth international congress of industrial medicine. 1948.
Proc. R. Soc. Med. Proceedings of the Royal Society of Medicine. London.
Proc. roy. Soc. Proceedings of the Royal Society. London.
Proc. Soc. exp. Biol., N. Y. Proceedings of the Society for Experimental Biology and Medicine. New York (Utica, N. Y.).
Proc. U. S. nav. Inst. Proceedings of the United States Naval Institute. Annapolis, Md.
Psychoanal. Quart. Psychoanalytic Quarterly. Albany, N. Y.
Psychoanal. Rev. Psychoanalytic Review. New York.
Psychol. Bull. Psychological Bulletin. Lancaster, Pa.
Psychol. Rev. Psychological Review. Lancaster, Pa.
Psychosom. Med. Psychosomatic Medicine. Experimental and Clinical Studies. Washington.
Publ. Hlth., Lond. Public Health. London.
Publ. Hlth. Bull., Wash. Public Health Bulletin. Washington.
Publ. Hlth. Rep., Wash. Public Health Reports. Washington.

Quart. Bull. Nthwest. Univ. Quarterly Bulletin of Northwestern University. (b) Medical. Evanston, Ill.
Quart. J. exp. Physiol. Quarterly Journal of Experimental Physiology. London.
Quart. J. exp. Psychol. Quarterly Journal of Experimental Psychology. Cambridge.
Quart. J. Med. Quarterly Journal of Medicine. Oxford.
*Quart. Phi Beta Pi med. Frat.** Quarterly. Phi Beta Pi Medical Fraternity. Menasha, Wis.

Radiology. Radiology. Syracuse, N. Y.
Rass. ital. Otorinolaring. Rassegna italiana di oto-rino-laringologia. Napoli.
Rass. Med. industr. Rassegna di medicina industriale. Torino.
Res. Rev. Research Reviews. London.
Research, Lond. Research: a journal of science and its applications.
Res. Quart. Amer. Phys. Educ. Ass. Research Quarterly of the American Physical Education Association. Ann Arbor.
Rev. argent. Dermato-sif. Revista argentina de dermato-sifilologica. Buenos Aires.
Rev. belge Path. Revue belge de pathologie et de médecine expérimentale. Bruxelles.
Rev. canad. Biol. Revue canadienne de biologie. Montréal.
Rev. gén. Clin. Revue génerale de clinique et de therapeutique. Paris.
Rev. méd. Nancy. Revue médicale de Nancy.
Rev. Méd. nav. Revue de médecine navale (métropole et outremer). Paris.
Rev. oto-neuro-oftal., B. Aires. Revista oto-neuro-oftalmológica y de cirurgia neurológica. Buenos Aires.
Rev. Otorinolaring., Santiago. Revista de otorinolaringologia. Santiago de Chile.
Rev. Sanid. Aero., B. Aires. Revista de sanidad de aeronáutica. Buenos Aires.
Rev. sci. Instrum. Review of Scientific Instruments. New York.
Ric. sci. Mem. Ricerca scientifica (e reconstruzione) Memorie. Roma.
Rinsyo & Kenkyo. Japanese Journal of Clinical and Experimental Medicine. Hokuoka.
Riv. Med. aero. Rivista di medicina aeronautica. Roma.
Roy. Nav. med. Bull. Royal Naval Medical Bulletin. London.

Scand. J. clin. lab. Invest. Scandinavian Journal of Clinical and Laboratory Investigation. Oslo.
Schweiz. Arch. Neurol. Psychiat. Schweizer Archiv für Neurologie und Psychiatrie. Zurich.
Schweiz. med. Wschr. Schweizerische medizinische Wochenschrift. Basel.
Sci. Amer. Scientific American. New York.
Sci., Ill. Science. Illinois.
Sci. Mon., N. Y. Scientific Monthly. New York.
Sci. News Lett., Wash. Science News Letter. Washington.
Science. Science. New York.
Sem. Hôp. Paris. Semaine des hôpitaux de Paris.

Settim. med. Settimana medica. Palermo.
*Soc. med. tskr.** Social medicinsk tidskrift. Stockholm.
Sovetsk. Vrach. Zh. Sovetskiy vrachebniy zhurnal. Leningrad.
Sth. med. J., Birmingham. Southern Medical Journal. Journal of the Southern Medical Association. Birmingham, Ala.
Strasbourg-med. Strasbourg-médical. Strasbourg.
Stud. Rockefeller Inst. med. Res. Studies from the Rockefeller Institute for Medical Research, New York.
Summ. Diss. Northw. Univ. Summaries of Dissertations. Northwestern University, Chicago.
Surg. Gynec. Obstet. Surgery, Gynecology and Obstetrics. Chicago.
Svenska Läkartidn. Svenska Läkartidningen. Stockholm.

*Tech. Data Dig. U. S. Air Cps.** Technical Data Digest. U. S. Air Corps. Dayton, Ohio.
Terap. Arkh. Terapevticheskii Archiv. Moskva.
Tex. Rep. Biol. Med. Texas Reports on Biology and Medicine. Galveston.
Ther. Umsch. Therapeutische Umschau. Bern.
Thorax. Thorax. London.
Tidskr. milit. Hälsov. Tidskrift i militär hälsovård. Stockholm.
Tidsskr. norske Laegeforen. Tidsskrift for den Norske Laegeforening. Kristiania, Kjøbenhavn.
Tohoku J. exp. Med. Tohoku Journal of Experimental Medicine. Sendai.
Toulouse méd. Toulouse médical. Toulouse.
Trans. Amer. Acad. Ophthal. Otolaryng. Transactions of the American Academy of Ophthalmology and Oto-laryngology. St. Louis.
Trans. Amer. climat. (clin.) Ass. Transactions of the American Climatological (and Clinical) Association. Philadelphia.
Trans. Amer. laryng. rhin. otol. Soc. Transactions of the American Laryngological, Rhinological and Otological Society. New York.
Trans. Amer. ophthal. Soc. Transactions of the American Ophthalmological Society. New York.
Trans. Amer. otol. Soc. Transactions of the American Otological Society. Boston.
Trans. Amer. Soc. Heat. Vent. Engrs. Transactions of the American Society of Heating and Ventilating Engineers. New York.
Trans. Ass. Amer. Phycns. Transactions of the Association of American Physicians. Philadelphia.
Trans. med. engr. Ind. Hyg. Found. Transactions, medical and engineering section. Transaction Series, Bulletin no. 3 Industrial Hygiene Foundation. Pittsburgh.
Trans. R. Soc. trop. Med. Hyg. Transactions of the Royal Society of Tropical Medicine and Hygiene. London.
Tufts med. J. Tufts medical Journal. Boston.
Turk Tip Cem. Mec. Turk Tip cemiyeti mecmuasi. Istanbul.

Ugeskr. Laeg. Ugeskrift for Laeger. Kjøbenhavn.
Univ. Qd. Dept. Physiol. University of Queensland Papers. Department of Physiology.
U. S. Forces med. J. United States Armed Forces Medical Journal. Washington.

Verh. dtsch. path. Ges. Verhandlungen der Deutschen Pathologischen Gesellschaft. Jena.
Virchows Arch. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin. Berlin.
Vjschr. schweiz. Sanitoff. Vierteljahrsschrift für Schweizerische Sanitatoffiziere. Basel.
Volta Rev. Volta Review. Washington.
Vyestn. Otorhinolaryng., Leningr. Vyestnik Otorhinolaryngologii. Leningrad.

W. Va. med. J. West Virginia Medical Journal. Wheeling.
War. Med., Chicago. War Medicine. Chicago.
Wis. med. J. Wisconsin Medical Journal. Milwaukee.

Yale J. Biol. Med. Yale Journal of Biology and Medicine. New Haven. Conn.

Z. Biol. Zeitschrift für Biologie. Berlin & München.
u. ges exp. Med. Zeitschrift für die gesamte experimentelle Medizin. Berlin.
Z. Hals– Nas.– u. Ohrenheilk. Zeitschrift für Hals– Nasen– und Ohrenheilkunde. München & Berlin.

KEY TO AGENCY ABBREVIATIONS

In listing reports from a given source the abbreviations in the corporate entries and serial listings have been adopted from those employed by the agency; when these were lacking, a suitable abbreviation has been devised by the authors. An alphabetical listing of all such abbreviations follows, together with a few additional symbols. The italicized words in each case form the basis of the abbreviation.

AAF	U. S. *Army air forces.*
ACAMR	Canada. National research council of Canada. *Associate committee on aviation medical research.*
AMRL	U. S. Army service forces. *Armored medical research laboratory, Fort Knox, Ky.*
APU	Gt. Brit. Medical research council. *Applied psychology unit.* Psychological laboratory, Cambridge.
ASF	U. S. *Army service forces.*
BuAer	U. S. Navy. *Bureau of aeronautics.*
BuMed	U. S. Navy. *Bureau of medicine and surgery.*
BuNavPers	U. S. Navy. *Bureau of naval personnel.*
BuShips	U. S. Navy. *Bureau of ships.*
BuY & D	U. S. Navy. *Bureau of Yards and Docks.*
CAM	U. S. National research council. *Committee on aviation medicine.*
CES	Gt. Brit. Medical research council. Royal naval personnel research committee. *Climatic efficiency subcommittee.*
CUW	U. S. National research council. *Committee on undersea warfare.*
EDU	U. S. Navy. Naval Gun Factory. *Experimental diving unit.*
ENG	U. S. Air force. Air technical service command. *Engineering division.*
FPRC	Gt. Brit. Royal Australian air force. *Flying personnel research committee.*

HS — Gt. Brit. Medical research council. Royal naval personnel research committee. *Habitability subcommittee.*
MRC — Gt. Brit. *Medical research council.*
NATB — U. S. Navy. Pensacola, Fla. *Naval air training base.*
NDRC — U. S. office of scientific research and development. *National defense research committee.*
NEL — U. S. Navy. *Naval electronics laboratory, San Diego, Calif.*
NHMRC — Australia. *National health and medical research council.*
NMRI — U. S. Navy. *Naval medical research institute, Bethesda, Md.*
NRC — *National research council.*
NRL — *U. S. Navy. Naval research laboratory, Anacostia, D. C.*
OES — Gt. Brit. Medical research council. Royal naval personnel research committee. *Operational efficiency subcommittee.*
ONI — U. S. Navy. *Office of naval intelligence.*
ONR — U. S. Navy. *Office of naval research.*
OpNav — U. S. Navy. *Office of the chief of naval operations.*
OSRD — U. S. *Office of scientific research and develment.*
RNPRC — Gt. Brit. Medical research council. *Royal naval personnel research committee.*
SS — Gt. Brit. Medical research council. Royal naval personnel research committee. *Survival subcommittee.*
TSEAL — U. S. Air force. *Air technical service command. Engineering division. Aero medical laboratory.*
UPS — Gt. Brit. Medical research council. Royal naval personnel research committee. *Underwater physiology subcommittee.*
USAF — *U. S. Air force.*
UWB — Gt. Brit. Medical research council. Royal naval personnel research committee. *Underwater blast subcommittee.*
VPS — Gt. Brit. Medical research council. Royal naval personnel research committee. *Visual problems subcommittee.*

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